

Gaps X X - 0 Conservative Substitutions
 PGPiH |||||
 PGPiH X X

2. US-09-095-639A-1 (1-5)

aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5
 ID AAW31287 standard; peptide; 5 AA.XX
 AC AAW31287;
 XX
 DT 05-MAR-1998 (first entry)
 XX
 Bos taurus.

Bovine beta casein variant A1 immunogenic peptide motif.

XX
 KW variant beta casein; immunogenic; molecular mimicry; cow;
 KW milk product; insulin-dependent diabetes; GLUT2; diet.
 XX
 OS Bos taurus.XX
 PN W09724371-A1.
 XX
 PD 10-JUL-1997.
 XX
 PF 27-DEC-1996;
 XX
 PR 27-DEC-1995; 96WO-EP05846.
 XX
 PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LIGU.
 PA (MIDI-) MIDIA LTD.
 XX
 PI Pozzilli P;
 XX
 DR WPI; 1997-363622/33.XX
 PT Beta-casein or fragments not showing mimicry with GLUT2 - used in
 PT food or pharmaceutical products for prevention of insulin dependent
 PT diabetes, particularly in early infancy
 XX
 PS Claim 5; Page 3; 34pp; English.XX
 CC This sequence represents an immunogenic peptide motif from the A1
 GLUT2 protein found in insulin producing cells of the pancreas. There is
 a known correlation between exposure to cow's milk and the development of
 insulin-dependent diabetes which could possibly be linked to this
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk
 CC substantially free of non-human beta casein or containing modified
 CC beta-casein without this motif could be used in diets for the prevention
 XX
 SQ Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114

Initial Score 5
 Residue Identity 100%
 Gaps 0Optimized Score 5
 Matches 5
 Conservative Substitutions 0Significance 1.11
 Mismatches 0XX
 CC This sequence represents an immunogenic peptide motif from the A1
 GLUT2 protein found in insulin producing cells of the pancreas. There is
 a known correlation between exposure to cow's milk and the development of
 insulin-dependent diabetes which could possibly be linked to this
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk
 CC substantially free of non-human beta casein or containing modified
 CC beta-casein without this motif could be used in diets for the prevention
 XX
 SQ Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114

Initial Score 5
 Residue Identity 100%
 Gaps 0Optimized Score 5
 Matches 5
 Conservative Substitutions 0Significance 1.11
 Mismatches 0XX
 PGPiH |||||
 PGPiH X X3. US-09-095-639A-1 (1-5)
 R95509 Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.

AC R95609;

DT 26-NOV-1996 (first entry)

DE Bovine beta casein A1 variant.

KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;

KW butter; cheese; cream.

OS Bos taurus.

FH Key

FT region

PN W09614577-A1.

PD 17-MAY-1996.

PF 03-NOV-1995; NZ0114.

PR 04-NOV-1994; NZ-26-862.

PS (NACH-) NAT CHILD HEALTH RES FOUND.

PA (NZDA-) NEW ZEALAND DAIRY BOARD.

PI Elliott RB, Hill JP;

DR WPI: 96-251-885/25.

PT Selecting non-diabetogenic milk and milk prods. - by testing milk or
 cows for the presence of non-diabetogenic variants of beta-casein

PS Disclosure; Figure 2; 28pp; English.

CC A method for selecting milk for feeding to diabetes susceptible

CC individuals comprises testing milk from identified cows for the

CC presence of variants of beta casein and selecting those cows whose

CC milk contains non-diabetogenic variants and milking these cows

CC separately. The milk and milk products obtained can reduce the risk

CC of susceptible individuals contracting Type-1 diabetes.

SQ Sequence 209 AA.

SQ 5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 5 G; 6 H;

SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;

CC Retrieved by bobryen on Thu 27 Feb 103 16:22:05-PST using FindSeq

60 X X X 70

X X

PGPiH

|||||

AQTSQSLVPPPGPPGPHNSLPQNTIPPL

4. US-09-095-639A-1 (1-5)
 R80281 Meth1 or ethyl esterified bovine beta-casein A1.

ID R80281 standard; protein; 209 AA.

AC R80281;

DT 14-FEB-1996 (first entry)

DE Methyl or ethyl esterified bovine beta-casein A1.

KW Bovine; beta-casein; thyl esterification; pepsin hydrolysis;

KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.

OS Bos taurus.

FH Key

FT protein

FT 1..409

/note= "55% esterified by methanol or by

ethanol, resulting in atypical pepsin

cleavage sites, in addition to the

naturally occurring (native) sites"

4..5

/note= "pepsin cleavage site in native protein"

5..6

/note= "pepsin cleavage site in native protein and

in methyl ester of beta-casein"

11..12

/note= "newly identified pepsin cleavage site in

methyl ester of beta-casein."

15..16

/note= "pepsin cleavage site in native protein"

44..45

```

T cleavage_site
T   T   note= "pepsin cleavage site in native protein"
T   T   45..46 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   55..56 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   57..58 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   58..59 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   72..73 note= "pepsin cleavage site in native protein"
T   T   73..74 note= "newly identified pepsin cleavage site in
T   T   methyl ester of beta-casein"
T   T   80..81 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   93..94 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   125..126 note= "pepsin cleavage site in native protein"
T   T   126..127 note= "pepsin cleavage site in native protein"
T   T   127..128 note= "pepsin cleavage site in native protein"
T   T   141..142 note= "pepsin cleavage site in native protein"
T   T   142..143 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   156..157 note= "newly identified pepsin cleavage site in
T   T   ethyl ester of beta-casein"
T   T   160..163 note= "newly identified pepsin cleavage site in
T   T   ethyl ester of beta-casein"
T   T   163..164 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   164..165 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   188..189 note= "pepsin cleavage site in native protein and
T   T   in methyl ester of beta-casein"
T   T   189..190 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   190..191 note= "pepsin cleavage site in native protein and
T   T   in ethyl ester of beta-casein"
T   T   191..192 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   192..193 note= "pepsin cleavage site in native protein and
T   T   in methyl and ethyl esters of beta-casein"
T   T   198..199 note= "newly identified pepsin cleavage site in
T   T   methyl and ethyl esters of beta-casein"
T   T   207..208 note= "newly identified pepsin cleavage site in
T   T   methyl ester of beta-casein"
T   peptide
T   FT   2..25 /label= A
T   FT   26..28 /label= B
T   peptide
T   FT
T   peptide
T   FT

```

PGPIH
 |||||
 AQTOSLVYPFPGPPIHNSLPQNIPPL
 60 X X 70

5. US-09-095-639A-1 (1-5)
 aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

XX ID AAR95609 standard; protein; 209 AA.

XX AC AAR95609;

XX DT 26-NOV-1996 (first entry)

XX DE Bovine beta casein A1 variant.

XX KW Milk; beta casein; diabetogenic; diabetes; cow; milk products; butter; cheese; cream.

XX Bos taurus.

XX Key Location/Qualifiers

FT 63 .68 /label= Diabetogenic hexapeptide.

XX PN WO9614577-A1.

XX PD 17-MAY-1996.

XX PR 03-NOV-1995; 95WO-NZ00114.

XX PR 04-NOV-1994; 94NZ-0264962.

XX PA (NACH-) NAT CHILD HEALTH RES FOUND.

XX PA (NZDA-) NEW ZEALAND DAIRY BOARD.

XX PI E11101TT RB, H111 JP;

XX DR; 1996-251805/25.

XX PT Selecting non-diabetogenic milk and milk prods. - by testing milk or

XX PT cows for the presence of non-diabetogenic variants of beta-casein

XX PS Disclosure; Figure 2; 28pp; English.

CC A method for selecting milk for feeding to diabetes susceptible

CC individuals comprises testing milk from identified cows for the presence of variants of beta casein and selecting those cows whose

CC milk contains non-diabetogenic variants and milking these cows

CC separately. The milk and milk products obtained can reduce the risk

CC of susceptible individuals contracting Type-1 diabetes.

XX SQ Sequence 209 AA.

XX AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014

XX Initial Score = 5 Optimized Score = 5 Significance = 1.11

XX Residue Identity = 100% Matches = 5 Mismatches = 0

XX Gaps = 0 Conservative Substitutions = 0

XX X X PGPIH
 |||||

AQTOSLVYPFPGPPIHNSLPQNIPPL
 60 X X 70

6. US-09-095-639A-1 (1-5)

W31289 Bovine beta casein variant A1 immunogenic Peptide.

ID W31289 standard; peptide; 12 AA.

AC W31289;

DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A1 immunogenic peptide.

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.

PD 10-JUL-1997;

PF 27-DEC-1996; E05846.

PR 27-DEC-1995; IT-ITM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MIDI-) MIDIA LTD.

PI Porzilli P;

DR WPI; 97-36322/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

PT food or pharmaceutical products for prevention of insulin dependent

PT diabetes, particularly in early

PT infancy

CC This sequence represents an immunogenic peptide from the A1 variant of

CC beta-casein which contains a motif (see W31287) capable of mimicking a

CC fragment of the GLUT2 protein found in insulin producing cells of the

CC pancreas. There is a known correlation between exposure to cow's milk and

CC the development of insulin-dependent diabetes which could possibly be

CC linked to this molecular mimicry. Dietary or pharmaceutical products

CC derived from milk substantially free of non-human beta-casein or

CC for the prevention of insulin dependent diabetes particularly during

CC early infancy.

CC Sequence 12 AA;

CC SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;

CC 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;

CC Retrieved by boberry on Thu 27 Feb 103 16:22:07-PST using FindSeq

CC Initial Score = 5 Optimized Score = 5 Significance = 1.11

CC Residue Identity = 100% Matches = 5 Mismatches = 0

CC Gaps = 0 Conservative Substitutions = 0

CC X X PGPIH
 |||||

SLVPPPGPPIIN

X 10

7. US-09-095-639A-1 (1-5)

aaW31289 Bovine beta casein variant A1 immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.

XX XX AAW31289;

AC AC

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A1 immunogenic peptide.

XX KW A1 variant beta casein; immunogenic; molecular mimicry; cow;

XX milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.

PD 10-JUL-1997.

PF 27-DEC-1996; 96WO-EP05846.

PR 27-DEC-1995; 95IT-0RM0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

CC development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta-casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

CC Sequence 12 AA;

CC 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;

CC 0 L; 1 K; 0 M; 1 F; 4 P; 1 T; 0 W; 1 Y; 1 V;

CC Retrieved by boberry on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00

Residue Identity = 80% Matches = 4 Mismatches = 0

Gaps = 0 Conservative Substitutions = 1

X X
PGPIH
| | |
SLVYPPFGPGIPN
X 10

13. US-095-639a-1 (1-5)
aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; Peptide; 12 AA.

AC AAW31290;

XX 05-MAR-1998 (first entry)

DE Bovine beta casein variant A2 immunogenic peptide.

XX A2 variant beta-casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

OS Bos indicus.

XX WO9724371-A1.

XX 27-DEC-1995; 951T-0R0550.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.
(MDI-) MIDIA LTD.

PA Pottzilli P;

XX WPI: 1997-363622/33.

DR This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide contains a motif (see AAW31288) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during infancy.

CC This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide contains a motif (see AAW31288) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during infancy.

CC early infancy.

CC Sequence 12 AA;

CC AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..

Initial Score = 4 Optimized Score = 4 Significance = 0.00

Residue Identity = 80% Matches = 4 Mismatches = 0

Gaps = 0 Conservative Substitutions = 1

X X
PGPIH
| | |
SLVYPPFGPGIPN
X 10

14. US-095-639a-1 (1-5)
Beta casein precursor.

P02666 check: 8112 from: 1 to: 224 AA.

TOIG of: P02666 check: 8112 from: 1 to: 224 AA.

ID CASB_BOVIN STANDARD; PRT; 224 AA.

AC P02666; Created)

DT 21-JUL-1986 (Rel. 01, Last sequence update)

DT 01-MAR-1989 (Rel. 10, Last annotation update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Beta casein precursor.

GN CSN2.

OS Bos taurus (Bovine). Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae; Bovidae; Bovinae; Bos.

NCBL TAXID=9913;

RN [1]

SEQUENCE FROM N.A.

RX MEDLINE=80188989; PubMed=2833669;

RA Baev A.A., Smirnov I.K., Gorodetsky S.I.; Willis I.M., Shah F., Beattie C.W., DE Beta casein precursor.

RT "Primary structure of bovine beta-casein cDNA.";

RL CSN2.

OS Eukaryota; Metazoa; OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae; Bovinae; Bos.

RN [2]

SEQUENCE FROM N.A.

RX MEDLINE=80188989; PubMed=2833669;

RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M., RN [3]

RA Mackinlay A.G.; RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein cDNAs: comparisons with related sequences in other species.";

RT Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.; RN [4]

RA "Complete nucleotide sequence of the bovine beta-casein gene.";

RT RNL Mol. Biol. Evol. 4:231-241(1987).

RN [5]

SEQUENCE FROM N.A.

RX MEDLINE=90147219; PubMed=3271384;

RA Jimenez-Flores R., Ring J.M., Stewart A.F., Mackinlay A.G.; RT "Cloning and sequence analysis of bovine beta-casein cDNA.";

RT Blochem. Biophys. Res. Commun. 142:617-621(1987).

RN [6]

SEQUENCE FROM N.A. (VARIANT A3).

RC TISSUE-Mammary Gland;

RX MEDLINE=94068382; PubMed=3248100;

RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G., RT "Overproduction of bovine beta-casein in Escherichia coli and engineering of its main chymosin cleavage site.";

RT Protein Eng. 6:763-770(1993).

RN [7]

SEQUENCE OF 16-224 (VARIANT A2).

RP MEDLINE=8152525; PubMed=327893;

RX Carles C., Huet J.-C., Ribadeau-Dumas B.; RT "A new strategy for primary structure determination of proteins:

application to bovine beta-casein.";
FEBS Lett. 229:265-272(1988).
RN [7]

SEQUENCE OF 16-224 (VARIANT A2);
MEDLINE=72233212; PubMed=4557764;
RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;
"Primary structure of bovine beta casein. Complete sequence.";
RL Eur. J. Biochem. 25:505-514(1972).
RN [8]

VARIANTS A1; B AND C;
MEDLINE=72214259; PubMed=5064450;
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;
"Characterization of genetic variants of alpha-S1 and beta bovine
caseins.";
RT EUR. J. Biochem. 26:328-337(1972).
RN [9]

SEQUENCE OF 118-124 (VARIANT A3);
RX MEDLINE=71252171; PubMed=4397616;
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;
RT "Localization in the peptide chain of bovine beta casein of the
His/Gln substitution differentiating the A2 and A3 genetic
variants";
C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).
RN [10]

SEQUENCE OF 48-63 (VARIANT E);
RX MEDLINE=75005247; PubMed=441121;
RA Grosclaude F., Judinkova F.S., Gorodetsky S.I.;
"Identification of bacterial clones encoding bovine caseins by direct
immunological screening of the cDNA library.";
RT EUR. J. Biochem. 32:381-388(1984).
RN [11]

SEQUENCE OF 68-105 FROM N.A.;
RX MEDLINE=85155504; PubMed=6397405;
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
Sulimova G.E., Judinkova F.S., Gorodetsky S.I.;
"Identification of bacterial clones encoding bovine caseins by direct
immunological screening of the cDNA library.";
RT EUR. J. Biochem. 145:3-5(1974).
RN [12]

SEQUENCE OF 68-95 FROM N.A.;
RX MEDLINE=86014005; PubMed=3900695;
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
Sulimova G.E.;
RT "Identification of bacterial clones coding for bovine caseins by
direct immunologic screening of the cDNA library.";
RL Mol. Biol. (Mosk) 19:955-963(1985).
RN [13]

SEQUENCE OF 18-57 FROM N.A. AND SEQUENCE OF 16-224 (VARIANT H).
RX MEDLINE=20154951; PubMed=10690361;
RA Han S.K., Shin Y.C., Byun H.D.;
"Biochemical, molecular and physiological characterization of a new
beta-casein variant detected in Korean cattle.";
Anim. Genet. 31:49-51(2000).
RN [14]

SEQUENCE OF 125-195 (VARIANT A1 AND G).
RX MEDLINE=26118672; PubMed=7496485;
RA Visscher S., Slanger C.J., Lagerwerf F.M., Van Dongen W.D.,
Havercamp J.;
RT "Characterization of a non-electrophoretic genetic variant of beta-
casein by peptide mapping and mass spectrometric analysis.";
Int. Dairy J. 8:967-972(1998).
RN [15]

SEQUENCE OF 160-171 (VARIANT F).
RX MEDLINE=8318023; PubMed=6397774;
RA Willis J.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;
"Construction and identification by partial nucleotide sequence
analysis of bovine casein and beta-lactoglobulin cDNA clones.";
RT

RL DNA 1:375-386(1982).
RN [17]

CARBONDRATE-LINKAGE SITES.
RP RX MEDLINE=85000478; PubMed=6148101;
RA Yan S.B., Wold F.;
RT "Neoglycoproteins: In vitro introduction of glycosyl units at
glutamines in beta-casein using transglutaminase.";
RL Biochemistry 23:3759-3765(1984).
CC "- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE
PROPERTIES OF THE CASEIN MICELLES.
CC "- SUBCELLULAR LOCATION: EXTRACELLULAR.
CC "- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC "- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190
AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS
THE A2 VARIANT.
CC "- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.
CC "- DATABASE: NAME=Protein Spottlight;
NOTE="Issue 16 of November 2001;
WWW="http://www.expasy.org/spottlight/articles/sptlt016.html".
CC

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CC

DR M1645; AAA30480.1;
EMBL; M15132; AAA30430.1;
DR K01087; AAA30481.1;
EMBL; K03539; AAA30482.1;
EMBL; M55158; AAA30431.1;
DR S67277; AAB29137.1;
EMBL; AY104929; AAD09813.1;
EMBL; AF104928; AAD09813.1;
DR M64756; AAB39254.1;
DR PIR; A23110; KBBOA2.
DR PIR; A23846; A2B5A6.
DR B22087; B29087.
DR PIR; S01860; S01860.
DR PIR; S02429; S02429.
DR CarbPro; CSDR0067;
DR InterPro; IPR001588; Casein.
DR Pfam; PF00363; casein; 1.
DR PROSITE; PS00306; CASTIN ALPHA BETA; 1.
KW MILK; Phosphorylation; Glycoprotein; Signal; Polymorphism.
FT SIGNAL 1 15
FT CHAIN 16 224 BETA CASEIN.
FT MOD RES 30 30
FT MOD RES 32 32
FT MOD RES 33 33
FT MOD RES 34 34
FT VARIANT 51 51
FT VARIANT 52 52
FT VARIANT 82 82
FT VARIANT 103 103
FT VARIANT 121 121
FT VARIANT 132 132
FT VARIANT 137 137
FT VARIANT 152 153
FT VARIANT 153 153
FT VARIANT 167 167
FT VARIANT 190 190
FT VARIANT 108 108
FT VARIANT 210 210
FT VARIANT 215 224

PHOSPHORYLATION.
PHOSPHORYLATION.
PHOSPHORYLATION (EXCEPT IN VARIANT C).
O-LINKED (GALNAC. . .). (PARTIAL).
O-LINKED (GALNAC. . .).
O-LINKED (GALNAC. . .).
O-LINKED (GALNAC. . .).
O-LINKED (GALNAC. . .).
R -> C (IN VARIANT H).
E -> K (IN VARIANT B).
E -> H (IN VARIANT C).
S -> R (IN VARIANT B).
LP -> PL (IN VARIANTS A1 AND H).
P -> L (IN VARIANT G).
P -> L (IN VARIANT F).
M -> E (IN VARIANTS A1 AND G).
L -> Q (IN VARIANT F).
E -> Q (IN REF. 4 AND 7).
PVRGPFIIV -> DPSLL (IN REF. 1).

RA Stewart A.F., Willis I.M., Mackinlay A.G.; and kappa-casein cDNAs.";
 RT "Nucleotide sequences of bovine alpha-S1- and kappa-casein genes.";
 RL Nucleic Acids Res. 12:3895-3907(1984).
 RN [21]

SEQUENCE FROM N.A. Nagao M., Makl M., Sasakai R., Chiba R.;
 RX Nagao M., Isolation and sequence analysis of bovine alpha-S1-casein cDNA clone.";
 RA Gorodetskii S.I., Zakharev V.M., Kyrashultsev D.R., Kapelinskaya T.V.;
 RA Skryabin K.G.;
 RT cDNA of cattle alpha S1-casein: cloning and nucleotide sequence.";
 RL [4]

SEQUENCE FROM N.A. MEDLINE-92051301; PubMed-1658736;
 RX Koczan D., Hobom G., Seydel H.M.;
 RA "Genomic organization of the bovine alpha-S1 casein gene.";
 RN [6] Nucleic Acids Res. 19:5591-5596(1991).
 RN SEQUENCE OF 55-120 FROM N.A. MEDLINE-83102023; PubMed-6897774;
 RX Thompson A.R., McKinlay A.G.;
 RA Willis I.M., Stewart A.F., Caputo A., Gorodetskii S.I.;
 RT "Construction and identification by partial nucleotide sequence
 RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";
 RT DNA 1:375-386(1982).
 RN [6]

SEQUENCE OF 122-214 FROM N.A. MEDLINE-05179833; PubMed-3038718;
 RX Kiarashultsev D.R., Zakharev V.M., Gorodetskii S.I.;
 RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of
 RT alpha S1-casein in cows.";
 RL Dok J. Akad. Nauk SSSR 280:1433-1437(1985).
 RN [17]

SEQUENCE OF 16-214 FROM N.A. MEDLINE-94154154; PubMed-1338277;
 RX Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;
 RT "Cloning, mapping, and sequencing of 3' and its flanking region of
 RT bovine alpha-S1 casein gene.";
 RL Chin. J. Biotechnol. 8:235-245(1992).
 RN [8]

SEQUENCE OF 16-214 (VARIANT B). MEDLINE-72063471; PubMed-4331376;
 RX Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;
 RT "Primary structure of bovine alpha-S1 casein. Complete sequence.";
 RT Eur. J. Biochem. 23:41-51(1971).
 RN [9]

REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).
 RX MEDLINE-74082545; PubMed-7497901;
 RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;
 RT Correction";
 RT Correction";
 RL Eur. J. Biochem. 40:323-323(1973).
 RN [10]

SEQUENCE (VARIANT D). MEDLINE-72214259; PubMed-5064450;
 RX Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RT "Primary structure of genetic variants of alpha-S1 and beta bovine
 RT caseins";
 RL Eur. J. Biochem. 26:328-337(1972).
 RN [11]

SEQUENCE OF 23-49 (VARIANT A).
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RT Localization in the N-terminal part of bovine casein alpha-S1 of a
 RT 13 amino-acid deletion that differentiates variant A from variants B
 RT and C.";
 RL FEMS Lett. 11:109-112(1970).
 RN [12]

SEQUENCE OF 205-214 (VARIANT C).
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RT

RT "On the localization in the C-terminal sequence of bovine casein alpha-S1 of a Glu/Gly substitution that differentiates the genetic variants B and C.";
 RL C. R. Acad. Sci., D., Sci. Nat. 271:563-563(1970).
 RN [13]

REVISION (VARIANT C).
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RL C. R. Acad. Sci., D., Sci. Nat. 271:563-563(1970).
 CC -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT
 CC -1- CALCIUM PHOSPHATE.
 CC -1- SUBCELLULAR LOCATION: Extracellular.
 CC -1- TISSUE/SPECIFICITY: MAMMARY GLAND; MILK.
 CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.
 CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.
 CC -1- DATABASE: NAME-Worthington enzyme manual;
 CC -1- WWW="http://www.worthington-biochem.com/manual/C/CASA.html";
 CC -1- DATABASE: NAME-Worthington Protein Spotlight;
 CC -1- NOTE="Issue 16 of November 2001";
 CC -1- WWW="http://www.exasy.org/spotlight/articles/sptlt016.html".
 CC -1-
 CC this SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation
 CC at the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by
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 CC or send an email to license@isb-sib.ch).
 CC -1-
 CC DR X00564; CRB57792; 1; -.
 CC DR M33123; AAA30428; 1; -.
 CC DR M36411; AAA30429; 1; -.
 CC DR X59854; CRB42516; 1; -.
 CC DR K01084; AAA30478; 1; -.
 CC DR M38655; AAA62707; 1; -.
 CC DR S72380; ADD14099; 1; -.
 CC DR P03106; KABOSB.
 CC DR PIR: A23071; S02202.
 CC DR PIR: S02202; S02202.
 CC DR PIR: S22575; S22575.
 CC DR InterPro: IPR001588; Casein.
 CC DR Pfam: PF00363; casein_1.
 CC DR PROSITE: PS00306; CASEIN_ALPHA_BETA; 1.
 CC KW MILK; Phosphorylation; Signal; Repeat.
 CC FT SIGNAL 1 15
 CC FT CHAIN 16 214
 CC FT MOD_RES 61 61
 CC FT MOD_RES 63 63
 CC FT MOD_RES 68 68
 CC FT MOD_RES 79 79
 CC FT MOD_RES 81 81
 CC FT MOD_RES 82 82
 CC FT MOD_RES 83 83
 CC FT MOD_RES 90 90
 CC FT MOD_RES 130 130
 CC FT REPEAT 85 99
 CC FT REPEAT 125 140
 CC FT VARIANT 29 41
 CC FT VARIANT 68 68
 CC FT VARIANT 207 207
 CC FT CONFLICT 42 42
 CC FT CONFLICT 50 50
 CC FT CONFLICT 95 95
 CC FT CONFLICT 143 143
 CC FT CONFLICT 203 203
 CC FT CONFLICT 211 212
 CC SEQUENCE 214 AA; 24529 MW; F066B5CAE55828B CRC64;
 P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..
 Initial Score = 3 Optimized Score = 4 Significance = 1.11
 Residue Identity = 60% Matches = 3 Mismatches = 2
 Gaps = 0 Conservative Substitutions = 0

X X
PGPIH
| |
YTDAPSFSDFDNPNTGSENSEKTTMP
190 200 X 210

18. US-09-095-639a-1 (1-5)
R37103 Bovine milk beta-casein enzymatic fragment.

ID R37103 standard; peptide: 7 AA.

AC R37103;

DT 21-MAY-1995 (first entry)

DE Bovine milk beta-casein enzymatic fragment.

KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders; wrinkles.

KW Bos Taurus.

OS J06166615-A.

PN J06166615-A.
PD 14-JUN-1994.

01-DEC-1992; 321624.
01-DEC-1992; JP-321624.

(PORK) POLA CHEM IND INC.
WPI: 94-230615/28.

DR PT Cosmetics for treating skin disorders and wrinkles - containing enzymatic hydrolysate of human or bovine milk beta-casein

PT Cosmetics for treating skin disorders and wrinkles - containing enzymatic hydrolysate of human or bovine milk beta-casein

Claim 2; Page 2; 7PP; Japanese.

CC The invention relates to cosmetics containing human or bovine milk beta-casein enzymatic hydrolysate. The cosmetics are used for improving skin disorders and/or wrinkles. They are more effective than previously used polysaccharides, sugar alcohols, glycerol,

CC glycols, etc.

CC The present sequence is one component of the bovine milk beta-casein enzymatic hydrolysate.

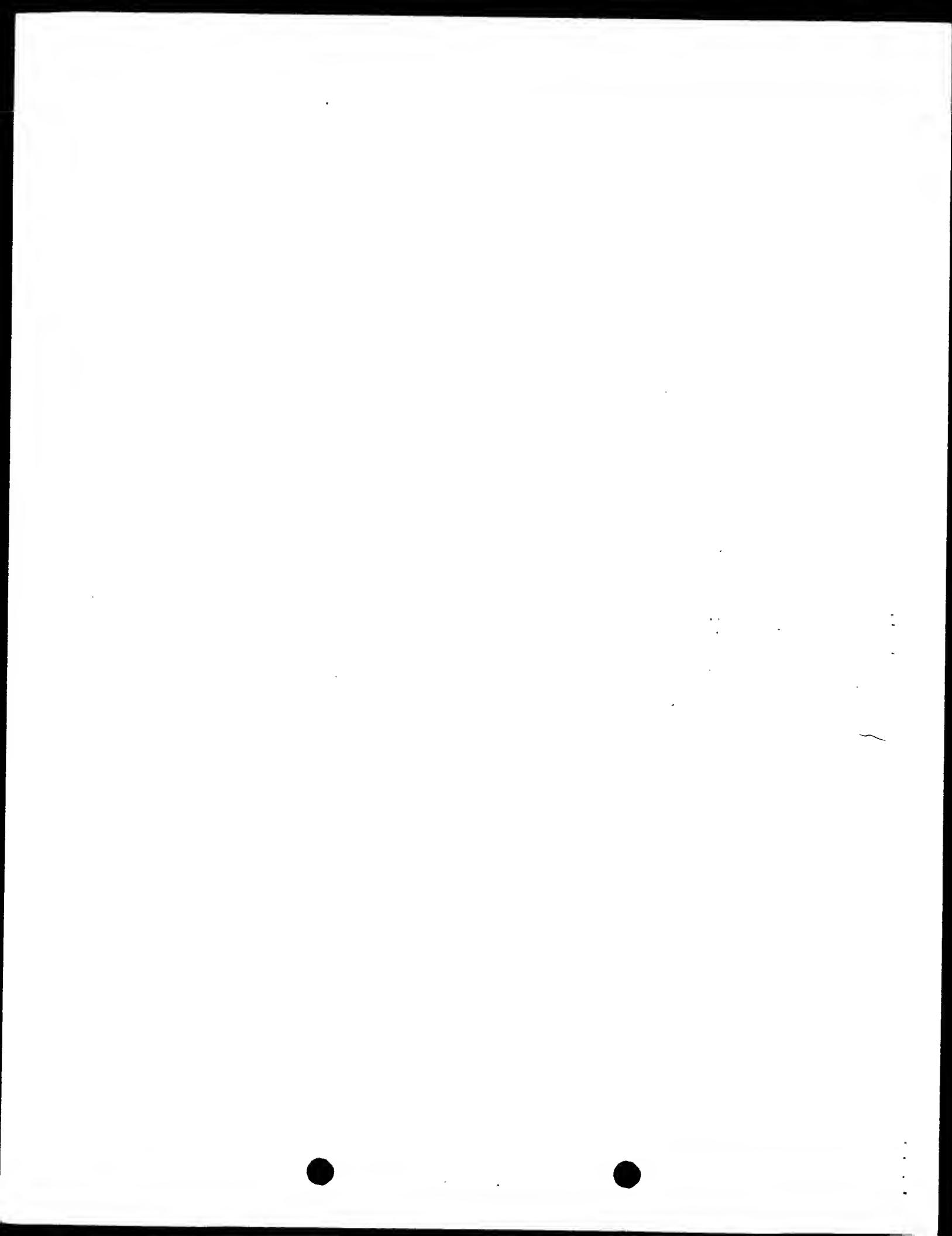
CC Sequence 7 AA;
SO 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;

SO 0 T; 0 I; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;

CC Retrieved by boobyren on Thu 27 Feb 103 16:22:04 PST using FindSeq

Initial Score = 2 Optimized Score = 3 Significance = -2.22
Residue Identity = 40% Matches = 2 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0

X X
PGPIH
| |
AVPYPOR
X X



Initial Score = 5 Optimized Score = 5 Significance = 1.19
 Residue Identity = 100% Matches = 5 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

X X PGP1P
 | | | | PGP1P
 X X X X

2. US-09-095-639a-2 (1-5)
 aaw31288 Bovine beta casein variant A2 immunogenic peptide
 TOIG of: aaw31288 check: 1154 from: 1 to: 5
 ID AAW31288 standard; peptide; 5 AA.
 XX AC AAW31288;
 DT 05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.
 A2 variant beta-casein; immunogenic; molecular mimicry; cow;
 KW milk product; insulin-dependent diabetes; GLUT2; diet.
 OS Bos taurus.
 OS Bos indicus.

XX PN W09724371-A1.
 XX PD 10-JUL-1997.
 XX PF 27-DEC-1996; 96WO-EP050546.
 XX PR 27-DEC-1995; 95IT-0RM0850.
 PA (BIOS-) BIOSISTEMA DI SARAPANTI & C SAS PIER LUIG.
 PA (MIDI-) MIDIA LTD.
 XX PT Pozzilli P;
 XX DR WPI; 1997-363622/33.
 XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in
 PT food or pharmaceutical products for prevention of insulin dependent
 PT diabetes, particularly in early infancy.

Claim 5; Page 4; 34pp; English.
 This sequence represents an immunogenic peptide motif from the A2 variant
 CC beta-casein found in both Bos taurus and Bos indicus (amino acid
 CC position 63-68). This motif is capable of mimicking a fragment of the
 CC GLUT2 protein found in insulin producing cells of the pancreas. There is
 CC a known correlation between exposure to cow's milk and the development of
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk
 CC substantially free of non-human beta casein or containing modified
 CC beta-casein without this motif could be used in diets for the prevention
 CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 5 AA:

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154 ..

Initial Score = 5 Optimized Score = 5 Significance = 1.0
 Residue Identity = 100% Matches = 5 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

X X PGP1P
 | | | | PGP1P
 X X X X

3. US-09-095-639a-2 (1-5)
 p02666 Beta casein precursor.
 TOIG of: p02666 check: 8112 from: 1 to: 224
 ID CASB_BOVIN STANDARD; PRT; 224 AA.
 AC P02666;
 DT 21-JUL-1986 (Rel. 01, Created)
 DR 01-MAR-1989 (Rel. 10, Last sequence update)
 DT 01-MAR-2002 (Rel. 41, Last annotation update)
 DE GN CSN2.
 OS Bos taurus (Bovine).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;
 OC Bovidae; Bovinae; Bos.
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Bev A.A., Smirnov I.K., Gorodetsky S.I.;
 RT "Primary structure of bovine beta-casein cDNA.";
 RL Mol. Biol. (Mosk) 21:214-222(1987).
 RN [2]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=88188969; PubMed=2833669;
 RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,
 RA Mackinlay A.G.;
 RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein."
 RL Mol. Biol. Evol. 4:231-241(1987).
 RN [3]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=20147279; PubMed=3271384;
 RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.,
 RT "Complete nucleotide sequence of the bovine beta-casein gene.";
 RL Aust. J. Biol. Sci. 41:527-537(1988).
 RN [4]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=87128158; PubMed=3814153;
 RA Jimenez-Flores R., Kang Y.C., Richardson T.;
 RT "Cloning and sequence analysis of bovine beta-casein cDNA."
 RL Biochem. Biophys. Res. Commun. 142:617-621(1987).
 RN [5]
 RP SEQUENCE FROM N.A. (VARIANT A3).
 RC TISSUE-Mammary Gland;
 RX MEDLINE=94068380; PubMed=8248100;
 RA Simons G., van den Heuvel W., Reynen T., Frijters A., Ruttens G.,
 RA Slanger C.J., Groenin M., de Vos W.M., Stezen R.J.;
 RT "Overproduction of bovine beta-casein in Escherichia coli and
 engineering of its main chymosin cleavage site."
 RL Protein Eng. 6:763-770(1993).
 RN [6]
 RP SEQUENCE OF 16-224 (VARIANT A2).
 RX MEDLINE=98115252; PubMed=377893;
 RA Cares C., Huot J.-C., Ribadeau-Dumas B.;
 RT "A new strategy for primary structure determination of proteins:
 application to bovine beta-casein.";
 RL FEBS Lett. 229:265-272(1988).
 RN [7]
 RP SEQUENCE OF 16-224 (VARIANT A2).
 RX MEDLINE=7223312; PubMed=4557764;
 RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.,
 RT "Primary structure of bovine beta casein. Complete sequence."
 RL Eur. J. Biochem. 25:505-514(1972).
 RN [8]
 RP VARIANT A1; B AND C.
 RX MEDLINE=72214229; PubMed=506450;
 RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;
 RT "Characterization of genetic variants of alpha-S1 and beta bovine

RT caseins."; Bur. J. Biochem. 26:328-337(1972).
 RL RN [9]
 RP SEQUENCE OF 118-124 (VARIANT A3); MEDLINE=7125211; PubMed=4997616;
 RX RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;
 RT "Localization in the peptide chain of bovine beta casein of the His-Gln substitution differentiating the A2 and A3 genetic variants."; C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).
 RL RN [10]
 RP SEQUENCE OF 48-63 (VARIANT E); MEDLINE=75005247; PubMed=4411121;
 RX RA Grosclaude F., Mahe M.-F., Voglino G.-F.;
 RT "The beta E variant and the phosphorylation code of bovine caseins."; FEBS Lett. 45:3-5(1974).
 RL RN [11]
 RP SEQUENCE OF 68-105 FROM N.A.; MEDLINE=85155504; PubMed=6397405;
 RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A., Silimova G.E., Judinkova E.S., Gorodetsky S.I.;
 RT "Identification of bacterial clones encoding bovine caseins by direct immunological screening of the cDNA library.";
 RT Gene 32:381-388(1984).
 RL RN [12]
 RP SEQUENCE OF 68-95 FROM N.A.; MEDLINE=86014005; PubMed=3900695;
 RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A., Silimova G.E.;
 RT "Identification of bacterial clones coding for bovine caseins by direct immunologic screening of the cDNA library.";
 RT RL Mol. Biol. (Mosk) 19:955-963(1985).
 RN [13]
 RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H); MEDLINE=20154951; PubMed=10690361;
 RA Han S.-K., Shin Y.C., Byun H.-D.;
 RT "Biochemical, molecular and physiological characterization of a new beta-casein variant detected in Korean cattle.";
 RL Anim. Genet. 31:49-51(2000).
 RN [14]
 RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).
 RA Dong C., Ng-Kwai-Hang K.F.;
 RA Visser S., Slanger C.J., Lagerwerf F.M., Van Dongen W.D., Haverkamp J.;
 RT "Characterization of a non-electrophoretic genetic variant of beta-casein by peptide mapping and mass spectrometric analysis.";
 RL Int. Dairy J. 8:967-972(1998).
 RN [15]
 RP SEQUENCE OF 160-171 (VARIANT F); MEDLINE=96118672; PubMed=496485;
 RL J. Chromatogr. A 711:141-150(1995).
 RA [16]
 RP SEQUENCE OF 170-184 FROM N.A.; MEDLINE=83182023; PubMed=897774;
 RX RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;
 RT "Construction and identification by partial nucleotide sequence analysis of bovine casein and beta-lactoglobulin cDNA clones.";
 RL DNA 1:375-386(1982).
 RN [17]
 RP CARBOHYDRATE-LINKAGE SITES; MEDLINE=85000478; PubMed=6148101;
 RX RA Yan S.B., Wold F.;
 RT "Noglycoproteins: in vitro introduction of glycosyl units at glutamines in beta-casein using transglutaminase.";
 RL Biochemistry 23:3759-3765(1984).
 CC -1- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE PROPERTIES OF THE CASEIN MICELLES.
 CC -1- SUBCELLULAR LOCATION: Extracellular.
 CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
 CC -1- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190

AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS THE A2 VARIANT.
 -1- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.
 -1- DATABASE: NAME=Protein Spotlight;
 NOTE=Issue 16 of November 2001;
 WWW=<http://www.expasy.org/spotlight/articles/sptlt016.html>.
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 CC EMBL; M16645; AAA30480.1;
 DR EMBL; M15132; AAA30430.1;
 DR EMBL; K01087; AAA30481.1;
 DR EMBL; X06359; CAA39658.1;
 DR EMBL; M55158; AAA30431.1;
 DR EMBL; S67277; AAB29137.1;
 DR EMBL; AF104929; AAD09813.1;
 DR EMBL; AF104928; AAD09813.1; JOINED.
 CC EMBL; M64756; AAB39524.1;
 DR PIR; A03110; KB0042.
 DR PIR; A25846; A25846.
 DR PIR; B29067; B29087.
 DR PIR; S01860; S01860.
 DR PIR; S02429; S02429.
 DR CarDBank; CICSD:9067;
 DR InterPro; IPR01588; Casein.
 DR Pfam; PF00363; caseins.1.
 DR PROSITE; PS00306; CASEIN_ALPHABETA; 1.
 KW KW; Phosphorylation; Glycoprotein; Signal; Polymorphism.
 FT SIGNAL 1 15
 FT CHAIN 16 224 BETA CASEIN.
 FT MOD_RES 30 30 PHOSPHORYLATION.
 FT MOD_RES 32 32 PHOSPHORYLATION.
 FT MOD_RES 33 33 PHOSPHORYLATION.
 FT MOD_RES 34 34 PHOSPHORYLATION.
 FT MOD_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).
 FT CARBOHYD 70 70 O-LINKED (GALNAC. . .) (PARTIAL).
 FT CARBOHYD 72 72 O-LINKED (GALNAC. . .).
 FT CARBOHYD 95 95 O-LINKED (GALNAC. . .).
 FT CARBOHYD 183 183 O-LINKED (GALNAC. . .).
 FT VARIANT 40 40 C (IN VARIANT H).
 FT VARIANT 51 51 E -> K (IN VARIANT E).
 FT VARIANT 52 52 E -> K (IN VARIANT C).
 FT VARIANT 82 82 P -> H (IN VARIANT A, B, C, F AND G).
 FT VARIANT 103 103 L -> I (IN VARIANT H).
 FT VARIANT 121 121 L -> Q (IN VARIANT A3).
 FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).
 FT VARIANT 137 137 S -> R (IN VARIANT B).
 FT VARIANT 152 152 S -> P (IN VARIANTS A1 AND H).
 FT VARIANT 153 153 P -> L (IN VARIANT G).
 FT VARIANT 167 167 P -> L (IN VARIANT F).
 FT VARIANT 190 190 E -> E (IN VARIANTS A1 AND G).
 FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).
 FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).
 FT CONFLICT 215 224 PVRGFEPITV -> DPSLL (IN REF. 1).
 SQ SEQUENCE 224 AA; F0BBDD8148A238AE CRC64;
 P02666 Length: 224 February 28, 2003 14:33 type: P Check: 8112 ..
 Initial Score = 5 Optimized Score = 5 Significance = 1.19
 Residue Identity = 100% Matches = 5 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

X X
 XGPPIP
 |||||
 AUTOSLYVYPFPPIPNSLPQNIPPL
 70 80 X 90

4. US-09-095-639A-2 (1-5)
aaW31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; peptide; 12 AA.
XX

AC AAW31290;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A2 immunogenic peptide.

XX DE A2 variant beta-casein; molecular mimicry; cow;

XX KW milk product; insulin-dependent diabetes; GLUT2; diet; 12 AA.

XX OS Bos taurus.

XX OS Bos indicus.

XX WO9724371-A1.

PD 10-JUL-1997.

XX PF 27-DEC-1996; 96W0-EP05846.

XX PR 27-DEC-1995; 95IT-0R06050.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX WPI: 1997-363622/33.

XX DR

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 5; Page 4; 34pp; English.

XX CC This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide

CC contains a motif (see AAW31290) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived

CC from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early

XX infancy.

XX Sequence 12 AA;

XX

CC This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide

CC contains a motif (see AAW31290) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived

CC from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early

XX infancy.

XX SQ Sequence 12 AA;

XX AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..

XX Initial Score = 5 Optimized Score = 5 Significance = 1.19
XX Residue Identity = 100% Matches = 5 Mismatches = 0
XX Gaps = 0 Conservative Substitutions = 0

XX X

XX PGPIP

XX |||||

XX SLVYBPFPPIPNN

XX X 10

XX 5. US-09-095-639A-2 (1-5)
W31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; peptide; 12 AA.

AC W31290;

DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A2 immunogenic peptide.

XX KW milk product; insulin-dependent diabetes; GLUT2; diet; 12 AA.

XX OS Bos taurus.

XX OS Bos indicus.

XX WO9724371-A1.

PD 10-JUL-1997.

XX PF 27-DEC-1996; 96W0-EP05846.

XX PR 27-DEC-1995; IT-RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI: 97-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp; English.

XX CC This sequence represents an immunogenic peptide found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is

ID W31290 standard; peptide; 12 AA.

AC W31290;

DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A2 immunogenic peptide.

XX KW A2 variant beta-casein; molecular mimicry; cow;

XX KW milk product; insulin-dependent diabetes; GLUT2; diet; 12 AA.

XX OS Bos taurus.

XX OS Bos indicus.

XX WO9724371-A1.

PD 10-JUL-1997.

XX PF 27-DEC-1996; 96W0-EP05846.

XX PR 27-DEC-1995; IT-RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI: 97-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

XX food or pharmaceutical products for prevention of insulin dependent

XX diabetes, particularly in early infancy

XX PS Claim 5; Page 4; 34pp; English.

XX CC This sequence represents an immunogenic peptide from the A2 variant of

CC beta-casein found in both Bos taurus and Bos indicus. The peptide

CC contains a motif (see AAW31290) corresponding to amino acids 63-68 of the

CC A2 beta casein protein and is found to be capable of mimicking a

CC fragment of the GLUT2 protein found in insulin producing cells of the

CC pancreas. There is a known correlation between exposure to cow's milk and

CC the development of insulin-dependent diabetes which could possibly be

CC linked to this molecular mimicry. Dietary or pharmaceutical products

CC derived from milk substantially free of non-human beta casein or

CC containing modified beta-casein without this motif could be used in diets

CC for the prevention of insulin dependent diabetes particularly during

CC early infancy.

XX SQ Sequence 12 AA;

XX AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..

XX Initial Score = 5 Optimized Score = 5 Significance = 1.19
XX Residue Identity = 100% Matches = 5 Mismatches = 0
XX Gaps = 0 Conservative Substitutions = 0

XX X

XX PGPIP

XX |||||

XX SLVYBPFPPIPNN

XX X 10

XX 6. US-09-095-639A-2 (1-5)

W31294 Bovine beta casein immunogenic peptide motif 2.

ID W31294 standard; peptide; 4 AA.

AC W31294;

DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein immunogenic peptide motif 2.

XX KW Beta-casein; immunogenic; molecular mimicry; cow;

XX KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX KW OS Bos taurus.

XX OS Bos indicus.

XX WO9724371-A1.

PD 10-JUL-1997.

XX PF 27-DEC-1996; 96W0-EP05846.

XX PR 27-DEC-1995; IT-RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI: 97-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

XX food or pharmaceutical products for prevention of insulin dependent

XX diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp; English.

XX CC This sequence represents an immunogenic peptide found in bovine

CC beta casein. This motif is capable of mimicking a fragment of the

CC GLUT2 protein found in insulin producing cells of the pancreas. There is

KW Al variant beta casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin dependent diabetes; GLUT2; diet.

XX Bos taurus.

OS WO9724371-A1.

XX PN 10-JUL-1997.

XX PD 27-DEC-1996; 96WO-EP05846.

XX PF 27-DEC-1995; 95IT-ORM0850.

XX DE (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.
PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR WPI; 1997-363622/33.

XX PS Beta casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 5; Page 3; 34pp; English.

XX CC This sequence represents an immunogenic peptide motif from the Al variant of beta casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 5 AA;

XX W31289 Length: 5 March 3, 2003 11:29 type: P Check: 1114 ..

Initial Score = 4 Optimized Score = 4 Significance = 0.00
Residue Identity = 80% Matches = 4 Mismatches = 1
Gaps = 0 Conservative Substitutions = 0

XX X
PGPPIP
| | |
PGPPIH
X X

XX W31289 US-095-639A-2 (1-5) Bovine beta casein variant Al immunogenic peptide.

AC W31289 standard; peptide: 12 AA.

DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant Al immunogenic peptide.

KW Al variant beta casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.

PD 10-JUL-1997; E05946.

PR 27-DEC-1995; IT-RM0850.
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.
PA (MIDI-) MIDIA LTD.

PI POZZILLI P;

DR WO9724371-A1.

PR Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 3; 34pp; English.

CC This sequence represents an immunogenic peptide from the Al variant of beta casein which contains a motif (see W31287) capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

CC Sequence 12 AA;
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 H;
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 PST using Findseq

Initial Score = 4 Optimized Score = 4 Significance = 0.00
Residue Identity = 80% Matches = 4 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0

XX X
PGPPIP
| | |
SLVYFPGPPIH
X 10

11. US-095-639A-2 (1-5)
aaW31289 Bovine beta casein variant Al immunogenic peptide.

TOIG of: aaw31289 Check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide: 12 AA.

AC AAW31289;

AC AAW31289;

XX DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant Al immunogenic peptide.

XX KW Al variant beta casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN WO9724371-A1.

XX PD 10-JUL-1997.

XX PR 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-0RM0850.

XX PR 27-DEC-1995; 95IT-0RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR 1997-363622/33.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR 97-363622/33.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR 97-363622/33.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR 97-363622/33.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI POZZILLI P;

XX DR 97-363622/33.

CC This sequence represents an immunogenic peptide from the Al variant of beta-casein which contains a motif (see W31287) capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas.

CC There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

CC Sequence 12 AA;

CC SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 H;

CC SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;

CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 PST using Findseq

Initial Score = 4 Optimized Score = 4 Significance = 0.00
Residue Identity = 80% Matches = 4 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0

XX X
PGPPIP
| | |
SLVYFPGPPIH
X 10

diets for the prevention of insulin dependent diabetes particularly during early infancy.

Bos taurus.
Key

of susceptible individuals contracting Type-1 diabetes.

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X X X X

PGP/IP

ESTATE PLANNING FOR THE RETIREMENT OF A COUPLE

卷之三

US-09-095-639A-2 (1-5)

R80281 Methyl or ethyl esterified bovine beta-casein A1.

R00281 Standard; protein; 209 AA.
R00281.

14-FEB-1996 (first entry)
Methyl or ethyl esterified bovine beta-casein Al.
bovine; beta-casein; ethyl esterification; pepsin hydrolysis;
proteins; non-dairy; food; observations

Location/Qualifiers
 1..209
 /note= "55% esterified by methanol or by ethanol, resulting in atypical pepsin cleavage sites, in addition to the naturally occurring (native) sites"
 4..5
 /note= "pepsin cleavage site in native protein"
 5..6
 /note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
 11..12
 /note= "newly identified pepsin cleavage site in methyl ester of beta-casein"
 15..16
 /note= "pepsin cleavage site in native protein"
 44..45
 /note= "pepsin cleavage site in native protein"
 45..46
 /note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
 55..56
 /note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
 57..58
 /note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
 58..59
 /note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
 72..73
 /note= "pepsin cleavage site in native protein"
 73..74
 /note= "newly identified pepsin cleavage site in methyl ester of beta-casein"
 80..81
 /note= "pepsin cleavage site in native protein and in methyl and ethyl esters of beta-casein"
 125..126
 /note= "pepsin cleavage site in native protein"
 126..127
 /note= "pepsin cleavage site in native protein"
 127..128
 /note= "pepsin cleavage site in native protein"
 141..142
 /note= "pepsin cleavage site in native protein"
 142..143
 /note= "newly identified pepsin cleavage site in methyl and ethyl esters of beta-casein"
 162..163
 /note= "newly identified pepsin cleavage site in ethyl ester of beta-casein"
 163..164
 /note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
 188..189
 /note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
 189..190
 /note= "pepsin cleavage site in native protein and in methyl and ethyl esters of beta-casein"
 190..191

The native form of bovine beta-casein A1 contains various Pepsin cleavage sites. Esterification of the protein with methanol or ethanol results in a form of beta-casein contg. additional, non-conventional Pepsin cleavage sites (see Features table). Esterified peptides and amino acids (and their mixtures) resulting from hydrolysis of an esterified protein (pref. beta-lactoglobulin or beta-casein) are claimed. The hydrolysis products are useful as ingredients, sequences or active agents in foods, pharmaceuticals and cosmetics.

Sequence 209 AA;
 SO 5 A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;
 SO 10 I; 22 L; 11 R; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
 CC Retrieved by boobyren on Thu 27 Feb 103 16:22:04 PST using Findseq
 CC
 Initial Score = 4 Optimized Score = 4 Significance = 0.00
 Residue Identity = 80% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

X X
 PGTP
 || || |
 AQIQSLVYYPFPFPFHNSLFQNTIPPL
 60 X X 70

14. US-09-095-632A-2 (1-5)
 aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209
 ID AAR95609 standard; protein; 209 AA.
 XX
 AC AAR95609;
 XX
 DT 26-NOV-1996 (first entry)
 XX Bovine beta casein A1 variant.
 XX KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;
 XX KW butter; cheese; cream.
 XX OS Bos taurus.
 XX FH Location/Qualifiers
 XX Region 63 .88
 XX FT /label= Diabetogenic hexapeptide.
 XX PN W09614577-A1.
 XX PD 17-MAY-1996.
 XX 03-NOV-1995; 95WO-NZ00114.
 XX PR 04-NOV-1994; 94NZ-0264862.
 XX PA (NZCH-) NAT CHILD HEALTH RES FOUND.
 XX PA (NZDA-) NEW ZEALAND DAIRY BOARD.
 XX PI Elliott RB, Hill JP;
 XX DR WPI; 1996-251885/25.
 XX PT Selecting non-diabetogenic milk and milk prods. - by testing milk or
 XX individuals comprises testing milk from identified cows for the
 XX presence of variants of beta casein and selecting those cows whose
 XX milk contains non-diabetogenic variants and milking these cows
 XX separately. The milk and milk products obtained can reduce the risk
 XX of susceptible individuals contracting Type-1 diabetes.

SO	Sequence	209 AA;	
AAR95609	Length: 209	March 3, 2003 11:28	Type: P Check: 2014 ..
Initial Score = 4	Optimized Score = 4	Significance = 0.00	
Residue Identity = 80%	Matches = 0	Conservative Substitutions = 1	
Gaps = 0		Mismatches = 0	
	X X PGPIP AQTSILVYPPFPQTHSNLPPNPL 60 X X 70		
15. US-09-095-639A-2 (1-5)	Bovine beta casein immunogenic peptide motif 1.		
W31293	Standard; Peptide; 4 AA.		
W31293	05-MAR-1998 (first entry)		
DE Bovine beta casein immunogenic peptide motif 1.			
KW Beta casein; immunogenic; molecular mimicry; cow;			
KW milk product; insulin-dependent diabetes; GLUT2; diet.			
GS Bos taurus.			
PN WO9724371-A1.			
PD 10-JUL-1997.			
PR 27-DEC-1995; E05846.			
PR 27-DEC-1995; IT-RM0850.			
PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.			
PA (MIDI-) MIDIA LTD.			
PI Pozzilli P;			
WPT; 97-363622/33.			
DR Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy			
PT Between exposure to cow's milk and the development of insulin dependent diabetes, particularly in early infancy			
PT This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes, particularly in early infancy			
PT This sequence represents an immunogenic peptide motif of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes, particularly in early infancy			
PS Claim 10, Page 6, 34pp; English.			
CC This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes, particularly in early infancy			
CC This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes, particularly in early infancy			
CC Dietary or pharmaceutical products derived from non-human beta casein or containing modified beta-casein motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy			
CC Dietary or pharmaceutical products derived from non-human beta casein or containing modified beta-casein motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy			
CC Sequence 4 AA:			
CC 0 A; 0 R; 0 N; 0 D; 0 C; 0 E; 0 Z; 1 G; 1 H;			
CC 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;			
CC Retrieved by boygen on Thu 27 Feb 103 16:22:07 -PST using FindSeq			
Initial Score = 3	Optimized Score = 3	Significance = -1.19	
Residue Identity = 75%	Matches = 3	Mismatches = 1	
Gaps = 0	Conservative Substitutions = 0		
	X X PGPIP X X		
17. US-09-095-639A-2 (1-5)	Bovine beta casein immunogenic peptide motif 1.		
TOIG of: P02662	check: 2471	from: 1 to: 214	
ID CAS1_BOVIN STANDARD;			
AC P02662; Q28048;			
AC 21-JUL-1986 (Rel. 01, Created)			
DT 01-NOV-1990 (Rel. 16, Last sequence update)			
DT 01-MAR-2002 (Rel. 41, Last annotation update)			
DE Alpha-S1 casein precursor.			
GN CSN1S1.			
OS Bos taurus (Bovine).			
OC Buxtorvaya; Metzora; Chordata; Craniata; Vertebrata; Eute-			
OC Mammalia; Eutheria; Chordata; Craniata; Vertebrata; Eute-			
OC Bovidae; Bovinae; Bos.			
OX NCBI_TAXID=9913;			
RN [1]			
RP SEQUENCE FROM N-terminus.			
RP RX			

RA Stewart A.F., Willis I.M., Mackinlay A.G.; "Nucleotide sequences of bovine alpha 1- and kappa-casein cDNAs.";
RT Nucleic Acids Res. 12:3895-3907(1984).
RL RN [2]
RP SEQUENCE FROM N.A.
RA Nagao M., Maki M., Sasakai R., Chiba R.; "Isolation and sequence analysis of bovine alpha-S1-casein cDNA clone.";
RT RN RT
RP Agric. Biol. Chem. 48:1663-1667(1984).
RN RN [3]
RP SEQUENCE FROM N.A. PubMed-3022833;
RX MEDLINE-87049835; Kyarshulite D.R., Kapelinskaya T.V., Gorodetskii S.I., Zakharev V.M.; "Cloning and nucleotide sequence of cattle alpha-S1-casein: cloning and nucleotide sequence.";
RA Skryabin K.G.; "CDNA of cattle alpha-S1-casein: cloning and nucleotide sequence.";
RL RN RT
RP SEQUENCE FROM N.A. PubMed-1658736;
RX MEDLINE-92051301; Pubmed-1658736;
RA Koczan D., Hobom G., Seyert H.M.; "Genomic organization of the bovine alpha-S1 casein gene.";
RN RN [4]
RP SEQUENCE OF 55-130 FROM N.A. PubMed-5897774;
RX MEDLINE-83182023; Pubmed-6897774;
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.; "Construction and identification by Partial nucleotide sequence analysis of bovine casein and beta-lactoglobulin cDNA clones.";
RT RN [5]
RP SEQUENCE OF 1222-214 FROM N.A. PubMed-3838718;
RX MEDLINE-85108933; Pubmed-3838718;
RA Klarshulite D.R., Zakharev V.M., Gorodetskii S.I.; "Nucleotide sequence of the 3'-nontranslated region of the mRNA of alpha-S1-casein in cows.";
RT RT
RA Dokh. Akad. Nauk SSSR 280:1433-1437(1985).
RL RN [6]
RP SEQUENCE OF 164-214 FROM N.A. PubMed-94154154; Pubmed-1343827;
RX Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.; "Cloning, mapping, and sequencing of 3' and its flanking region of bovine alpha-S1 casein gene.";
RT Chin. J. Biotechnol. 8:235-245(1992).
RN RN [7]
RP SEQUENCE OF 16-214 (VARIANT B).
RX MEDLINE-2063417; Pubmed-1331376;
RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.; "Primary structure of bovine alpha-S1 casein. Complete sequence.";
RT RT
RA "Primary structure of bovine alpha-S1 casein. Complete sequence.";
RL RN [8]
RP REVISIONS TO 74 AND 92-93 (VARIANT A; B; C AND D).
RX MEDLINE-1408545; Pubmed-1408545;
RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.; "Primary structure of alpha casein and of bovine beta casein. Correction.";
RT RT
RA Eur. J. Biochem. 40:323-323(1973).
RN RN [9]
RP SEQUENCE (VARIANT D).
RX MEDLINE-2214259; Pubmed-5064450;
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.; "Characterization of genetic variants of alpha-S1 and beta bovine caseins.";
RT RT
RA Eur. J. Biochem. 26:328-337(1972).
RL RN [10]
RP SEQUENCE OF 23-49 (VARIANT A).
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.; "Localization in the N-terminal part of bovine casein alpha-S1 of a 13 amino-acid deletion that differentiates variant A from variants B and C.";
RT RT
RA FEBS Lett. 11:109-112(1970).
RN RN [11]
RP SEQUENCE OF 205-214 (VARIANT C).
RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.; "Localization in the N-terminal part of bovine casein alpha-S1 of a 13 amino-acid deletion that differentiates variant A from variants B and C.";
RT RT
RA FEBS Lett. 11:109-112(1970).
RN RN [12]
RP SEQUENCE OF 205-214 (VARIANT C).
RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.; "Localization in the N-terminal part of bovine casein alpha-S1 of a 13 amino-acid deletion that differentiates variant A from variants B and C.";

RT "On the localization in the C-terminal sequence of bovine casein variants B and C.";
RT variants B and C.";
RT C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).
RL RN [13]
RP REVISION (VARIANT C).
RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.; "Characterization of genetic variants of alpha-S1 and beta bovine caseins.";
RT RT
RA C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).
RL CC
CC -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT CALCIUM PHOSPHATE.
CC CC
CC -1- SUBCELLULAR LOCATION: Extracellular.
CC CC
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC CC
CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.
CC CC
CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.
CC CC
CC -1- DATABASE: NAME-Worthington enzyme manual;
WWW-<http://www.worthington-biochem.com/manual/C/casein.html>;
NOTE=Issue 16 of November 2001;
WWW-<http://www.easy.org/spotlight/articles/spt1016.html>;
CC CC
CC This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation in the European Bioinformatics Institute. There are no restrictions on its use by non-profit institutions as long as its content is in no way modified and this statement is not removed. Usage by and for commercial entities requires a license agreement (see [http://www.lsbsib.ch/announce/](mailto:license@lsb-sib.ch) or send an email to license@lsb-sib.ch).
CC CC
CC DR X00564; CAB57792; 1;
EMBL M33123; AAA30428; 1;
DR DR
EMBL M58641; AAA30429; 1;
DR DR
EMBL X59856; CAA44516; 1;
DR DR
EMBL K01084; AAA30478; 1;
EMBL M38558; AAA62107; 1;
DR DR
EMBL S72388; AAD1099; 1;
PTR A03106; KABOSB.
PTR A23071;
DR DR
PIR S02202; S0202;
PIR S22575; S22575;
DR DR
InterPro IPR001588; Casein.
DR DR
Pfam PF00363; caseins; 1.
DR DR
PROSITE PS00306; CASEIN ALPHA_BETA; 1.
KW Milk; Phosphorylation; Signal; Repeat.
FT SIGNAL 15
FT CHAIN 16
FT MOD_CHAIN 61
FT MOD_RES 61
FT MOD_RES 63
FT MOD_RES 63
FT MOD_RES 68
FT MOD_RES 79
FT MOD_RES 81
FT MOD_RES 82
FT MOD_RES 83
FT MOD_RES 90
FT MOD_RES 130
FT REPEAT 85
FT REPEAT 99
FT REPEAT 125
FT REPEAT 140
FT VARIANT 29
FT VARIANT 41
FT VARIANT 68
FT VARIANT 68
FT VARIANT 207
FT VARIANT 207
FT CONFLICT 42
FT CONFLICT 42
FT CONFLICT 50
FT CONFLICT 95
FT CONFLICT 143
FT CONFLICT 203
FT CONFLICT 211
FT CONFLICT 211
SQ SEQUENCE 214 AA;
P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..
Initial Score = 3
Residue Identity = 60%
Gaps = 0
Optimized Score = 3
Matches = 3
MisMatches = 2
Significance = -1.9
Conservative Substitutions = 0

X X
PGPTP
| |
YTDAPSFSIDIPNPICSENSKTTMP
190 200 X 210

18. US-095-639A-2 (1-5)
R37103 Bovine milk beta-casein enzymatic fragment.

ID R37103 standard; peptide: 7 AA.
AC R37103;
DT 21-MAY-1995 (first entry)
DE Bovine milk beta-casein enzymatic fragment.
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;
KW wrinkles.
OS Bos Taurus.
PN J06166615-A.
PD 14-JUN-1994.
DR 01-DEC-1992; 321624.
PA (PORK) POLA CHEM IND INC.
WP; 94-230515/28.
PT Cosmetics for treating skin disorders and wrinkles - containing
enzymatic hydrolysate of human or bovine milk beta-casein
Claim 2; Page 2; 7pp; Japanese.
PS The invention relates to cosmetics containing human or bovine milk
beta-casein enzymatic hydrolysate. The cosmetics are used for
CC improving skin disorders and/or wrinkles. They are more effective
CC than previously used polysaccharides, sugar alcohols, glycerol,
CC glycols, etc.
CC The present sequence is one component of the bovine milk beta-casein
CC enzymatic hydrolysate.
SQ Sequence 7 AA;
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;
SQ 0 T; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;
CC Retrieved by bobbyen on Thu 27 Feb 103 16:22:04 -PST using Findseq

Initial Score = 2 Optimized Score = 3 Significance = -2.38
Residue Identity = 40% Matches = 2 Conservative Substitutions = 3
Gaps = 0 Mismatches = 0

X X
PGPTP
| |
AVPPQR
X X



> O <
O| 10 IntelliGenetics
> O <

FastDB - Fast Pairwise Comparison of Sequences

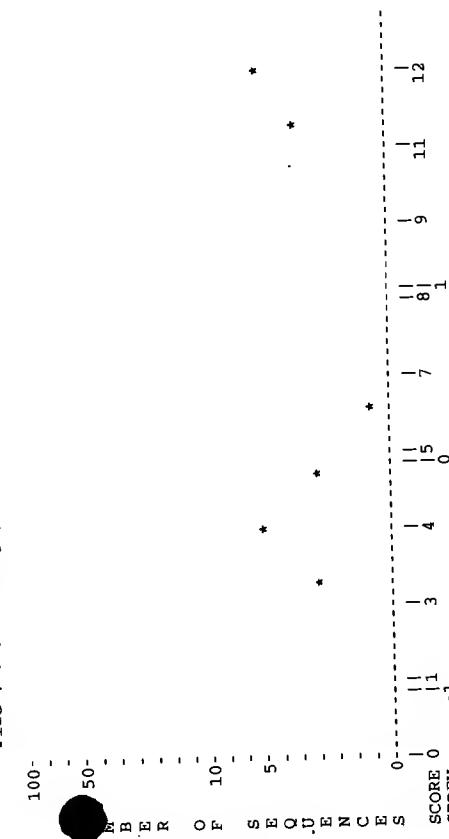
Release 5.4

Results file us-09-095-639a-3.res made by bobryen on Mon 3 Mar 103 11:49:27-PST.

Query sequence being compared:us-09-095-639a-3 (1-12)

Number of sequences searched: 18

Number of scores above cutoff: 18

Results of the initial comparison of us-09-095-639a-3 (1-12) with:
File : betabovine.pep

PARAMETERS

Similarity matrix PAM-150

Threshold level of sim. 16%

Match penalty 1

Mismatch penalty 5.00

Gap penalty 0.05

Cutoff score 0

Randomization group 0

SEARCH STATISTICS

Scores: Mean 7
Times: CPU 00:00:00.00Number of residues: 1156
Number of sequences searched: 18
Number of scores above cutoff: 18The scores below are sorted by initial score.
Significance is calculated based on initial score.
2 100% identical sequences to the query sequence were found:

Sequence	Name	Description	Length	Score	Init.	Opt.	Sig.	Frame
1.	W31289	Bovine beta casein variant A1	12	12	12	12	1.29	0
2.	aaw31289	Bovine beta casein variant A1	12	12	12	12	1.29	0
3.	R95609	Bovine beta casein A1 variant	209	12	12	12	1.29	0
4.	R80281	Methyl or ethyl esterified bo	209	12	12	12	1.29	0
5.	aar95609	Bovine beta casein A1 variant	209	12	12	12	1.29	0

1. W31289 Bovine beta casein variant A1
2. aaw31289 Bovine beta casein variant A1
3 100% similar sequences to the query sequence were found:

Sequence Name Description
1. W31289 Bovine beta casein variant A1
2. aaw31289 Bovine beta casein variant A1
3. R95609 Bovine beta casein A1 variant
4. R80281 Methyl or ethyl esterified bo
5. aar95609 Bovine beta casein A1 variant

The list of other best scores is:

Sequence Name	Description	Length	Score	Init.	Opt.	Sig.	Frame
1.	standard deviation above mean ***	12	11	11	11	1.03	0
2.	Bovine beta casein variant A2	12	11	11	11	1.03	0
3.	Bovine beta casein variant A2	224	11	11	11	1.03	0
4.	Beta casein precursor	214	6	7	0.26	0	
5.	Alpha-S1 casein precursor	214	6	5	5	0.52	0
6.	Bovine beta casein variant A1	5	5	5	5	0.52	0
7.	Bovine beta casein variant A1	5	5	5	5	0.52	0
8.	Bovine beta casein immunogeni	4	4	4	4	0.78	0
9.	Bovine beta casein immunogeni	5	4	4	4	0.78	0
10.	Bovine beta casein variant A2	5	4	4	4	0.78	0
11.	aaw31287	5	4	4	4	0.78	0
12.	W31193	5	4	4	4	0.78	0
13.	aaw1293	5	4	4	4	0.78	0
14.	W31288	5	4	4	4	0.78	0
15.	aaw31288	7	4	4	4	0.78	0
16.	R37103	7	4	4	4	0.78	0
17.	W31294	4	3	3	3	1.03	0
18.	aaw31294	4	3	3	3	1.03	0

1. US-09-095-639A-3 (1-12)
W31289 Bovine beta casein variant A1 immunogenic peptide.

ID W31289 standard; Peptide: 12 AA.
ID W31289; AC W31289; DT 05-MAR-1998 (first entry).
DE Bovine beta casein variant A1 immunogenic peptide.
KW Al variant beta casein; immunogenic; molecular mimicry; cow;
milk product; insulin-dependent diabetes; GLUT2; diet;
OS Bos taurus.
PN W0972471-A1.
PD 10-JUL-1997.
PR 27-DEC-1995; IT-RM0350.
(BIO-S-) BIOSISTEMA DI SARAPANTI & C SAS PIER LUIG.
PA (MDI-) MIDIA LTD.
PA Porzilli, P.
PI WPI; 97-363622/33.
DR Beta-casein or fragments not showing mimicry with GLUT2 - used in
PT food or pharmaceutical products for prevention of insulin dependent
PT diabetes particularly in early infancy
PS Claim 5; Page 3; 34pp; English.
CC This sequence represents an immunogenic peptide from the A1 variant of
beta-casein which contains a motif (see W31287) capable of mimicking a
fragment of the GLUT2 protein found in insulin producing cells of the
pancreas. There is a known correlation between exposure to cow's milk and
the development of insulin-dependent diabetes which could possibly be
linked to this molecular mimicry. Dietary or pharmaceutical products
derived from milk substantially free of non-human beta casein or
containing modified beta-casein without this motif could be used in diets
CC for the prevention of insulin dependent diabetes particularly during
CC early infancy.
Sequence 12 AA;
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-EST using FindSeq

Gaps = 0 Conservative Substitutions

X 10 X
SLVYPPGPTIN
| | | | | | | | | |
DKTHPFAOTOSLUVYPPGPTINSLPONIPPLT
X 60 70

5. US-09-095-639a-3 (1-12)
aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

ID AAR95609 standard; protein: 209 AA.
XX AAR95609;
AC XX
DT 26-NOV-1996 (first entry)
XX Bovine beta casein A1 variant.
KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;
butter; cheese; cream.
XX OS
XX Bos taurus.
XX Key Region 63...68
FT /label= Diabetogenic hexapeptide.
XX PN WO9614577-A1.
XX PD 17-MAY-1996.
XX PF 03-NOV-1995; 95WO-NZ00114.
XX PR 04-NOV-1994; 94NZ-0264862.
XX PA (NACH-) NAT CHILD HEALTH RES FOUND.
XX (NZDA-) NEW ZEALAND DAIRY BOARD.
PI Elliott RB, Hall JP;
XX WPI: 1996-251885/25.
XX Selecting non-diabetogenic milk and milk prods. - by testing milk or
cows for the presence of non-diabetogenic variants of beta-casein
XX Disclosure; Figure 2; 28PP; English.

CC A method for selecting milk for feeding to diabetes susceptible
CC individuals comprises testing milk from identified cows for the
CC presence of variants of beta casein and selecting those cows whose
CC milk contains non-diabetogenic variants and milking these cows
CC separately. The milk and milk products obtained can reduce the risk
CC of susceptible individuals contracting Type-1 diabetes.

XX Sequence 209 AA:
AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014
Initial Score = 12 Optimized Score = 12 Significance = 1.29
Residue Identity = 100% Matches = 12 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0

X 10 X
SLVYPPGPTIN
| | | | | | | | | |
DKTHPFAOTOSLUVYPPGPTINSLPONIPPLT
X 60 70

6. US-09-095-639a-3 (1-12)
W31290 Bovine beta casein variant A2 immunogenic peptide.

ID W31290 standard; peptide: 12 AA.
AC W31290;
DT 05-MAR-1998 (first entry)
DE Bovine beta casein variant A2 immunogenic peptide.
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;
milk product; insulin-dependent diabetes; GLUT2; diet.
OS Bos taurus.
OS Bos indicus.
PI Pozzilli P;
DR WO9724371-A1.
PT (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIGI.
PA (MIDI-) MIDIA LTD.
PI Pozzilli P;
DR WO9724372/33.
PT Beta-casein fragments not showing mimicry with GLUT2 - used in
PT food or pharmaceutical products for prevention of insulin dependent
PT diabetes, particularly in early infancy.
PT Claim 5; Page 4: 34pp; English.
CC This sequence represents an immunogenic peptide from the A2 variant of
beta-casein found in both Bos taurus and Bos indicus. The peptide
contains a motif (see W31288) corresponding to amino acids 63-68 of the
A2 beta casein protein and is found to be capable of mimicking
CC of the GLUT2 protein found in insulin producing cells of the pancreas.
CC There is a known correlation between exposure to cow's milk and the
CC development of insulin-dependent diabetes which could possibly be linked
CC to this molecular mimicry. Dietary or pharmaceutical products derived
CC from milk substantially free of non-human beta casein or containing
CC modified beta casein without this motif could be used in diets for the
CC prevention of insulin dependent diabetes particularly during early
CC infancy.
SQ Sequence 12 AA;
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using Findseq
Initial Score = 11 Optimized Score = 11 Significance = 1.03
Residue Identity = 91% Matches = 11 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0

X 10 X
SLVYPPGPTIN
| | | | | | | | | |
SLVYPPGPTIN
X 10 X

7. US-09-095-639a-3 (1-12)
aar31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aar31290 check: 6063 from: 1 to: 12
ID AAR31290 standard; peptide: 12 AA.
XX AC AAR31290;
XX DT 05-MAR-1998 (first entry)
XX DE Bovine beta casein variant A2 immunogenic peptide.
XX KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.
XX OS Bos taurus.
XX OS Bos indicus.
PN WO9724371-A1.
PD 1-0-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.
 XX
 PR 27-DEC-1995; 95IT-0RM0850.

PA (BIOS-) BIOSTIEMA DI SARAPANI & C SAS PIER LUIG.
 PA (MDI-) MIDIA LTD.
 PI Pozzilli P;
 XX DR WPZ; 1997-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 5; Page 4; 34pp; English.
 XX CC This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide contains a motif (see AAW31288) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 12 AA;
 AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..

Initial Score =	11	Optimized Score =	11	Significance =	1.03
Residue Identity =	91%	Matches =	11	Mismatches =	0
Gaps =	0	Conservative Substitutions =	1		

X 10 X
 SLYVPPGP1HN
 |||||11111|
 SLVYPPGP1PN
 X 10 X

8. US-09-095-639A-3 (1-12)
 p02666 Beta casein precursor.

DIG of: p02666 check: 8112 from: 1 to: 224

ID CASE_BOVIN
 AC P02666;
 DT 21-JUL-1986 (Rel: 01, Created)
 DT 01-MAR-1989 (Rel: 10, Last sequence update)
 DT 01-MAR-2002 (Rel: 41, Last annotation update)
 DE Beta casein precursor.

OS Bos taurus (Bovine).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;
 OC Bovidae; Bovinae; Bos.
 OX NCBI_TaxID=9913,

RN [1] SEQUENCE FROM N.A.
 RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;
 RT "Primary structure of bovine beta-casein cDNA.";
 RL Mol. Biol. (Mosk) 21:214-222(1987).

RN [2] SEQUENCE FROM N.A.
 RP MEDLINE=88189898; PubMed=2033669;
 RX Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M., Mackinlay A.G.;

RN [3] SEQUENCE FROM N.A.
RP MEDLINE=87049835; PubMed=3022833;
RX RA Skryabin K.G.;
RA "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence.";
RL BIokhimiia 51:1641-1648 (1986).
RN [4] SEQUENCE FROM N.A.
RP MEDLINE=92051301; PubMed=1658736;
RA "Genomic organization of the bovine alpha-S1 casein gene.";
RN [5] SEQUENCE OF 55-130 FROM N.A.
RP MEDLINE=83182023; PubMed=689774;
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;
RT "Construction and identification by partial nucleotide sequence
of bovine casein and beta-lactoglobulin cDNA clones.";
RN [6] SEQUENCE OF 122-214 FROM N.A.
RP MEDLINE=85178933; PubMed=3830718;
RA Kiarashulte D.R., Zahar'ev V.M.;
RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of
alpha S1-casein in cows";
RT "Cloning, mapping, and sequencing of 3' and its flanking region of
bovine alpha-S1 casein gene.";
RL Dokl. Akad. Nauk SSSR 280:1433-1437 (1985).
RN [7] SEQUENCE OF 164-214 FROM N.A.
RP MEDLINE=94154154; PubMed=1343827;
RX Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;
RT "Primary structure, mapping, and sequencing of 3' and its flanking region of
bovine alpha-S1 casein gene.";
RL Chin. J. Biotechnol. 8:325-325 (1992).
RN [8] SEQUENCE OF 16-214 (VARIANT B).
RP MEDLINE=2063417; PubMed=4331376;
-RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;
RT "Primary structure of bovine alpha-S1 casein. Complete sequence.";
RL Eur. J. Biochem. 23:41-51 (1971).
RN [9] REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).
RP MEDLINE=1408245; PubMed=4197901;
RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;
RT "Primary structure of alpha casein and of bovine beta casein.
Correction.";
RL Eur. J. Biochem. 40:323-323 (1973).
RN SEQUENCE (VARIANT D).
RP MEDLINE=72214259; PubMed=5064450;
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;
RT "Characterization of genetic variants of alpha-S1 and beta bovine
caseins";
RL Eur. J. Biochem. 26:328-337 (1972).
RN SEQUENCE OF 23-49 (VARIANT A).
RP Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;
RT "Localization in the N-terminal part of bovine casein alpha-S1 of a
13 amino-acid deletion that differentiates variant A from variants B
and C";
RL FEBS Lett. 11:109-112 (1970).
RN SEQUENCE OF 205-214 (VARIANT C).
RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
RA "On the localization in the C-terminal sequence of bovine casein
alpha-S1 of a Glu/Gly substitution that differentiates the genetic
variants B and C";
RL C. R. Acad. Sci., D, Sci. Nat. 271:563-563 (1970).
RN SEQUENCE (VARIANT C).
RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
RL C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136 (1970).
CC -1- SUBCELLULAR LOCATION: Extracellular.
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.
CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.
CC -1- DATABASE: NAME=Worthington enzyme manual;
CC WWW=http://www.worthington-biochem.com/manual/C/CASA.html".
CC -1- DATABASE: NAME=Protein Spotlight;
CC NOTE: Issue 16 of November 2001;
CC WWW=http://www.expasy.org/spotlight/articles/spt1t016.html".

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CC DR X00564; CAB7792_1; .
CC DR EMBL; M33123; ARN30428_1; .
CC DR EMBL; M38641; AAA30429_1; .
CC DR EMBL; X59855; CAA42516_1; .
CC DR EMBL; K01084; AAA30478_1; .
CC DR EMBL; M3158; AAA62707_1; .
CC DR EMBL; S72388; AAD14099_1; .
CC DR PIR; A31106; KABOB.
CC DR PIR; A23071; A23071.
CC DR PIR; S02202; S02202.
CC DR PIR; S22575; S22575.
CC DR InterPro; IPR01598; Casein.
CC DR Pfam; PF00363; caseins; 1.
CC DR PROSITE; PS00306; CASEIN_ALPHABETA; 1.
CC KW MILK; Phosphorylation; Signal; Repeat.
CC FT SIGNAL 1 15
CC FT CHAIN 16 214 ALPHA-S1 CASEIN.
CC FT MOD-RES 61 61 PHOSPHORYLATION.
CC FT MOD-RES 63 63 PHOSPHORYLATION.
CC FT MOD-RES 68 68 PHOSPHORYLATION.
CC FT MOD-RES 79 79 PHOSPHORYLATION.
CC FT MOD-RES 81 81 PHOSPHORYLATION.
CC FT MOD-RES 82 82 PHOSPHORYLATION.
CC FT MOD-RES 83 83 PHOSPHORYLATION.
CC FT MOD-RES 90 90 PHOSPHORYLATION.
CC FT MOD-RES 130 130 PHOSPHORYLATION.
CC FT REPEAT 85 99
CC FT REPEAT 125 140 MISSING (IN VARIANT A).
CC FT VARIANT 29 41
CC FT VARIANT 68 68 A->T (IN VARIANT D).
CC FT VARIANT 207 207 E->Q (IN VARIANT C).
CC FT VARIANT 42 42 P->L (IN REF. 3).
CC FT CONFLICT 50 50 P->L (IN REF. 4 AND 11).
CC FT CONFLICT 95 95 H->Q (IN REF. 5).
CC FT CONFLICT 143 143 H->D (IN REF. 3).
CC FT CONFLICT 203 203 S->L (IN REF. 6).
CC FT CONFLICT 211 212 MP->IS (IN REF. 3).
CC SQ SEQUENCE 214 AA: F056B5C9AE5528B CRC64;
P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..
Initial Score = 6 Optimized Score = 7 Significance = -0.26
Residue Identity = 168 Matches = 2 Mismatches = 10
Gaps = 0 Conservative Substitutions = 0

X SVYPPPPPIHN
MKLILITCLVAVALARPKHPIKHQGLPQEY
10 10 X
10 20

10. US-09-095-639A-3 (1-12)
W31287 Bovine beta casein variant A1 immunogenic peptide

Residue Identity = 100% Matches = 0

Conservative Substitutions = 4

Mismatches = 0

Gaps = 0

SLVYPPGPHTH
| | |
GPIH
X X13. US-09-095-639a-3 (1-12)
aaW31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaW31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

XX AAW31293;

XX 05-MAR-1998 (first entry)

Bovine beta casein immunogenic peptide motif 1.
XX Beta casein; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.
XX OS taurus.

XX PN WO974371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1995;

XX XX 96WO-EPO5846.

XX PR 27-DEC-1995;

XX 95IT-0RM0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUTIG.

XX (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR 1997-363622/33.

XX PR Beta-casein or fragments not showing mimicry with GLUT2 - used in
PT food or pharmaceutical products for prevention of insulin dependent
PT diabetes, particularly in early infancy

XX NS Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif of beta-casein
which is capable of mimicking a fragment of the GLUT2 protein found in
insulin producing cells of the pancreas. There is a known correlation
between exposure to cow's milk and the development of insulin-dependent
diabetes which could possibly be linked to this molecular mimicry.
Dietary or pharmaceutical products derived from milk substantially free
of non-human beta casein or containing modified beta-casein without this
motif could be used in diets for the prevention of insulin dependent
diabetes particularly during early infancy.

SQ Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738 ..
Initial Score = 4 Optimized Score = 4 Significance = -0.78
Residue Identity = 100% Matches = 0 Conservative Substitutions = 0
Gaps = 010
SLVYPPGPHTH
| | |
GPIH
X X14. US-09-095-639a-3 (1-12)
W31288 Bovine beta casein variant A2 immunogenic peptide

ID W31288 standard; peptide; 5 AA.

AC W31288;

DT 05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.
A2 variant beta-casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.
OS Bos taurus.

OS Bos indicus

PN WO974371-A1.

PD 10-JUL-1997.

PP 27-DEC-1996; E05846.

PR 27-DEC-1995; IT-RM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUTIG.

PA (MIDI-) MIDIA LTD.

PI Pozzilli P;

PP WPI: 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in
PT food or pharmaceutical products for prevention of insulin dependent
PT diabetes, particularly in early infancy
PS Claim 5; Page 4; 34pp; English.
CC This sequence represents an immunogenic peptide motif from the A2 variant
CC beta-casein found in both Bos taurus and Bos indicus (amino acid
CC position 63-68). This motif is capable of mimicking a fragment of the
CC GLUT2 protein found in insulin producing cells of the pancreas. There is
CC a known correlation between exposure to cow's milk and the development of
CC insulin-dependent diabetes which could possibly be linked to this
CC molecular mimicry. Dietary or pharmaceutical products derived from milk
CC substantially free of non-human beta casein or containing modified
CC beta-casein without this motif could be used in diets for the prevention
CC of insulin dependent diabetes particularly during early infancy.SQ Sequence 5 AA;
X 10 SLVYPPGPHTH
| | |
PPPIP
X XInitial Score = 4 Optimized Score = 4 Significance = -0.78
Residue Identity = 80% Matches = 4 Mismatches = 0
Gaps = 0 Conservative Substitutions = 0
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using Findseq15. US-09-095-639a-3 (1-12)
aaW31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaW31288 check: 1154 from: 1 to: 5

ID AAW31288 standard; peptide; 5 AA.

AC AAW31288;

XX DT 05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.
A2 variant beta-casein; immunogenic; molecular mimicry; cow;
KW milk product; insulin-dependent diabetes; GLUT2; diet.
OS Bos taurus.

OS Bos indicus

PN WO9724371-A1.

PD 10-JUL-1997.

XX

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

XX WO9724371-A1.

XX PN

XX 10-JUL-1997.

XX PD

XX 27-DEC-1996;

XX 96WO-EP05846.

XX PR

XX 27-DEC-1995;

XX 95IT-0RM0850.

XX (BOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MIDI-) MIDIA LTD.

XX

PI Pozzilli P;

XX DR WPI: 1997-363622/33.

XX

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX

PS Claim 10; Page 6; 34pp; English.

CC

This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

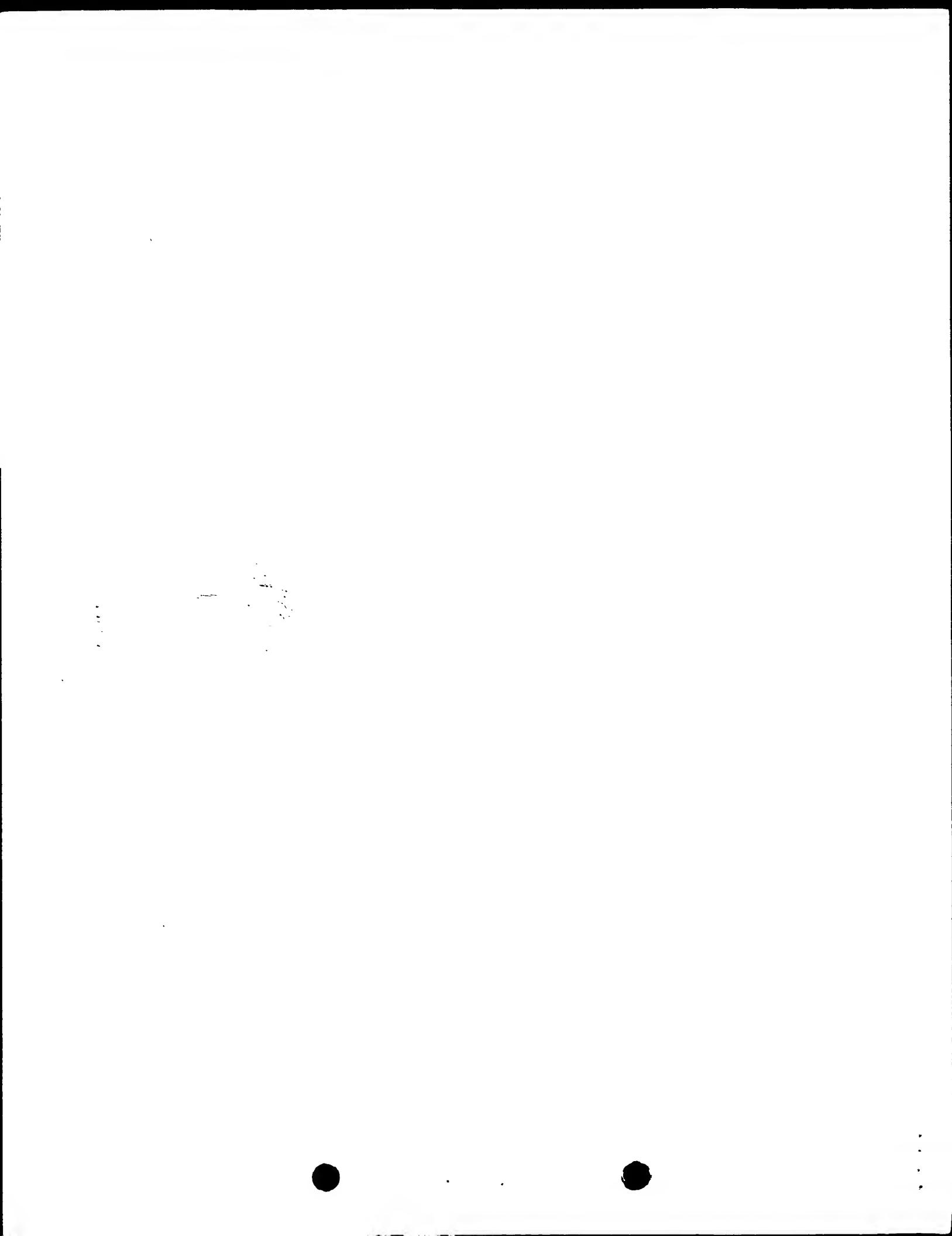
XX

SQ Sequence 4 AA;

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..
 Initial Score = 3 Optimized Score = 3 Significance = -1.03
 Residue Identity = 75% Matches = 3 Mismatches = 1
 Gaps = 0 Conservative Substitutions = 0

10

SLVYPPGPJHN
 |||
 GPPP
 x x



SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;
 CC Retrieved by bobjrey on Thu 27 Feb 103 16:22:07 -PST using FindSeq

Initial Score = 12 Optimized Score = 12 Significance = 1.33
 Residue Identity = 100% Matches = 12 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

X 10 X
 SLYVFPFPPIP
 1111111111
 SLYVFPFPPIP
 X 10 X

2. US-09-095-639A-4 (1-12)
 aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12
 AAW31290 standard; peptide; 12 AA.

AAW31290;

XX DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A2 immunogenic peptide.

XX KW A2 variant beta-casein; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX OS Bos indicus.

XX PN W0974371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996;

96WO-EP05846.

XX PR 27-DEC-1995;

95IT-ORM0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LIGU.

PA (MID-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI; 1997-363662/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both *Bos taurus* and *Bos indicus*. The peptide contains a motif (see AAW31298) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..
 Initial Score = 12 Optimized Score = 12 Significance = 1.33
 Residue Identity = 100% Matches = 12 Mismatches = 0

Gaps = - 0 conservative Substitutions = - 0

X 10 X
 SLYVFPFPPIP
 1111111111
 SLYVFPFPPIP
 X 10 X

3. US-09-095-639A-4 (1-12)
 p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB_BOVIN STANDARD; PRT; 224 AA.

AC P02666;
 DT 21-JUL-1986 (Rel. 01, Created)
 DT 01-MAR-1989 (Rel. 10, Last sequence update)
 DT 01-MAR-2002 (Rel. 41, Last annotation update)
 DE Beta casein precursor.
 GN CSN2.

OS Bos taurus (Bovine). Chordata; Craniata; Vertebrata; Euteleostomi; Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Bovidae; Bovidae; Bos. NCBI_TaxID=9913;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Bev A.A., Smirnov I.K., Gorodetsky S.I.;
 RA *Primary structure of bovine beta-casein cDNA.*;
 RT Mol. Biol. (Mosk) 21:214-222(1987).
 RN [2]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=88188989; PubMed=2833669;
 RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,
 RA Mackinlay A.G.;
 RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein cDNAs; comparisons with related sequences in other species.";
 RL Mol. Biol. Evol. 4:21-24(1987).
 RN [3]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=90147279; PubMed=3271384;
 RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;
 RT "Complete nucleotide sequence of the bovine beta-casein gene.";
 RL Aust. J. Biol. Sci. 41:527-537(1988).
 RN [4]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=87128156; PubMed=3814153;
 RA Jimenez-Flores R., Kang Y.C., Richardson T.;
 RA "Cloning and sequence analysis of bovine beta-casein cDNA.";
 RT "Complete nucleotide sequences of bovine beta-casein cDNA.";
 RL Biochem. Biophys. Res. Commun. 142:617-621(1987).
 RN [5]
 RP SEQUENCE FROM N.A. (VARIANT A3).
 RC TISSUE-Mammary gland;
 RX MEDLINE=94068388; PubMed=8248100;
 RA Simlons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,
 RA Slangen C.J., Groen M., de Vos W.M., Siezen R.J.;
 RT "Overproduction of bovine beta-casein in *Escherichia coli* and engineering of its main chymosin cleavage site.";
 RL Protein Eng. 6:763-770(1993).
 RN [6]
 RP SEQUENCE OF 16-224 (VARIANT A2).
 RX MEDLINE=88152254; PubMed=3278933;
 RA Carles C., Huet J.-C., Ribadeau-Dumas B.;
 RT "A new strategy for primary structure determination of proteins: application to bovine beta-casein.";
 RL FEBS Lett. 229:265-272(1988).
 RN [7]
 RP SEQUENCE OF 16-224 (VARIANT A2).
 RX MEDLINE=72233212; PubMed=455764;
 RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;
 RT "Primary structure of bovine beta casein. Complete sequence.";
 RL Eur. J. Biochem. 25:505-514(1972).

[8] RN VARIANTS A1; B AND C.
RP MEDLINE=72214259; PubMed=5064450;
RX Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;
RA "Characterization of genetic variants of alpha-S1 and beta bovine
caseins.";
RT Eur. J. Biochem. 26:328-337(1972);
RL RN SEQUENCE OF 118-124 (VARIANT A3);
RX MEDLINE=71225217; PubMed=4997616;
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;
RT "Localization in the peptide chain of bovine beta casein of the
His-Gln substitution differentiating the A2 and A3 genetic
variants.";
RT C. R. Acad. Sci., D, Sci. 270:2369-2372(1970).
RN [10] SEQUENCE OF 48-63 (VARIANT E).
RP MEDLINE=75005247; PubMed=4411121;
RX MEDLINE=75005247;
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;
RT "The beta E variant and the phosphorylation code of bovine caseins.";
FEBS Lett. 45:3-5(1974).
RN [11] SEQUENCE OF 68-105 FROM N.A.
RP MEDLINE=85155504; PubMed=6397405;
RX Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
RA Judinikova E.S., Gorodetskaya S.I.;
RT "Identification of bacterial clones encoding bovine caseins by direct
immunological screening of the cDNA library.";
RN Gene 32:381-388(1984).
RN [12] SEQUENCE OF 68-95 FROM N.A.
RP MEDLINE=86014005; PubMed=60069595;
RX Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,
RT "Identification of bacterial clones coding for bovine caseins by
direct immunologic screening of the cDNA library.";
RN [13] SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).
RP MEDLINE=20154951; PubMed=10690361;
RX Han S.K., Shin Y.C., Byun H.D.;
RA "Biochemical, molecular and physiological characterization of a new
beta-casein variant detected in Korean cattle.";
RT Anim. Genet. 31:49-51(2000).
RN [14] SEQUENCE OF 125-195 (VARIANTS A1 AND G).
RP DONG C., NG-KWAI-HANG K.F.;
RA "Characterization of a non-electrophoretic genetic variant of beta-
casein by peptide mapping and mass spectrometric analysis.";
RT Int. Dairy J. 8:967-972(1998).
RN [15] SEQUENCE OF 160-171 (VARIANT F).
RP MEDLINE=96118672; PubMed=1496485;
RA Visscher S., Sluangen C.J., Lagerwerf F.M., Van Dongen W.D.,
RA "Identification of a new generic variant of bovine beta-casein using
reversed-phase high-performance liquid chromatography and mass
spectrometric analysis.";
RT RL J. Chromatogr. A 711:141-150(1995).
RN [16] SEQUENCE OF 170-184 FROM N.A.
RP MEDLINE=83182023; PubMed=6897774;
RX WILLIIS I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;
RA "Construction and identification by partial nucleotide sequence
analysis of bovine casein and beta-lactoglobulin cDNA clones.";
RT DNA 1:375-386(1982).
RN [17] CARBOHYDRATE-LINKAGE SITES
RX MEDLINE=85000478; PubMed=6148101;
RA Yann S.B., Wold F.;
RT "Noglycycoproteins; in vitro introduction of glycosyl units at
RT glutamines in beta-casein using transglutaminase.";
RT Biochemistry 23:3759-3765(1984).

CC -!- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE
CC PROPERTIES OF THE CASEIN MICROFILS.
CC -!- SUBCELLULAR LOCATION: Extracellular.
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC -!- POLYMORPHISM: LEU15 IS PRESENT IN THE VARIANTS F AND G; GLN-190
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS
CC THE A2 VARIANT.
CC -!- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.
CC -!- DATABASE: NAME=Protein Spotlight;
CC NOTE=Issue 16 of November 2001;
CC WWW="http://www.eexpasy.org/spotlight/articles/spt016.html".
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation
CC at the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.ebi.ac.uk/announce/
CC or send an email to license@ebi.ac.uk).
CC -----
CC -----
CC DR EMBL: MI1645; AAA30480.1; JOINED.
CC DR EMBL: MI15132; AAA30430.1; JOINED.
CC DR EMBL: K01087; AAA30481.1; JOINED.
CC DR EMBL: X06359; CAA39658.1; JOINED.
CC DR EMBL: M55158; AAA30431.1; JOINED.
CC DR EMBL: S67277; AAB29137.1; JOINED.
CC DR EMBL: AF104929; AAD09813.1; JOINED.
CC DR EMBL: AF104928; AAD09813.1; JOINED.
CC DR EMBL: M64756; AAB89254.1; JOINED.
CC DR PIR: A03110; KBBOA2.
CC DR PIR: A23846; A25846.
CC DR PIR: B29087; B29087.
CC DR PIR: S01860; S01860.
CC DR PIR: S02429; S02429.
CC DR CarbBank; CCSD:9057; JOINED.
CC DR InterPro; IPR01588; Casein.
CC DR Pfam; PF00363; caseins; 1.
CC DR PROSITE; PS00306; CASEIN_ALPHA_BETA; 1.
CC KW MILK; Phosphorylation; Glycoprotein; Signal; Polymorphism.
CC FT SIGNAL 1 15
CC FT CHAIN 16 224
CC FT MOD_RES 30 30
CC FT MOD_RES 32 32
CC FT MOD_RES 33 33
CC FT MOD_RES 34 34
CC FT MOD_RES 50 50
CC FT CARBOHYD 70 70
CC FT CARBOHYD 72 72
CC FT CARBOHYD 95 95
CC FT CARBOHYD 183 183
CC FT VARIANT 40 40
CC FT VARIANT 51 51
CC FT VARIANT 52 52
CC FT VARIANT 82 82
CC FT VARIANT 103 103
CC FT VARIANT 121 121
CC FT VARIANT 132 132
CC FT VARIANT 137 137
CC FT VARIANT 152 153
CC FT VARIANT 153 153
CC FT VARIANT 167 167
CC FT VARIANT 190 190
CC FT VARIANT 190 190
CC FT CONFLICT 108 108
CC FT CONFLICT 210 210
CC FT CONFLICT 215 224
CC SQ SEQUENCE 224 AA; 25107 MW; 25107 MW; F0BDD8148A238AE CRC64;
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..

Initial Score = 12 Optimized Score = 12 Significance = 1.33
Residue Identity = 100% Matches = 12 Mismatches = 0
Gaps = 0

CC presence of variants of beta casein and selecting those cows whose
 CC milk contains non-diabetogenic variants and milking these cows
 CC separately. The milk and milk products obtained can reduce the risk
 CC of susceptible individuals contracting type-1 diabetes.

Sequence 209 AA:
 SQ 10 I; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;
 SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:05 PST using Findseq

Initial Score = 11 Optimized Score = 11 Significance = 1.06
 Residue Identity = 91% Matches = 11 Mismatches = 1
 Gaps = 0 Conservative Substitutions = 0

X 10 X
 SLWYPPGPIPN
 ||||| | | | | | | | |
 DKIHPFAQTOSLUVPPGPIPNLSPQNTIPPLT
 50 X 60 70

US-09-095-639A-4 (1-12)
 R80281 Methyl or ethyl esterified bovine beta-casein A1.

ID R80281; standard; protein; 209 AA.
 AC R80281;
 DT 14-FEB-1996 (first entry)
 DE Methyl or ethyl esterified bovine beta-casein A1.
 KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;
 KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.
 OS Bos taurus.
 FH Key Qualifiers
 FT protein 1..209
 /note= "55% esterified by methanol or by
 ethanol, resulting in atypical pepsin
 cleavage sites, in addition to the
 naturally occurring (native) sites"
 FT cleavage_site 11..12
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 4..5
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 5..6
 /note= "pepsin cleavage site in native protein and
 in methyl ester of beta-casein"
 FT cleavage_site 11..12
 /note= "newly identified pepsin cleavage site in
 methyl ester of beta-casein"
 FT cleavage_site 15..16
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 44..45
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 45..46
 /note= "pepsin cleavage site in native protein and
 in ethyl ester of beta-casein"
 FT cleavage_site 55..56
 /note= "pepsin cleavage site in native protein and
 in ethyl ester of beta-casein"
 FT cleavage_site 57..58
 /note= "pepsin cleavage site in native protein and
 in ethyl ester of beta-casein"
 FT cleavage_site 73..74
 /note= "newly identified pepsin cleavage site in
 methyl ester of beta-casein"
 FT cleavage_site 80..81
 /note= "pepsin cleavage site in native protein and
 in ethyl ester of beta-casein"
 FT cleavage_site 93..94
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 125..126
 /note= "pepsin cleavage site in native protein"

FT cleavage_site 126..127
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 127..128
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 141..142
 /note= "pepsin cleavage site in native protein"
 FT cleavage_site 142..143
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 156..157
 /note= "newly identified pepsin cleavage site in
 ethyl ester of beta-casein"
 FT cleavage_site 162..163
 /note= "newly identified pepsin cleavage site in
 ethyl ester of beta-casein"
 FT cleavage_site 163..164
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 164..165
 /note= "pepsin cleavage site in native protein and
 in ethyl ester of beta-casein"
 FT cleavage_site 188..189
 /note= "pepsin cleavage site in native protein and
 in methyl ester of beta-casein"
 FT cleavage_site 189..190
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 190..191
 /note= "pepsin cleavage site in native protein and
 in methyl ester of beta-casein"
 FT cleavage_site 191..192
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 192..193
 /note= "pepsin cleavage site in native protein and
 in methyl and ethyl esters of beta-casein"
 FT cleavage_site 198..199
 /note= "newly identified pepsin cleavage site in
 methyl and ethyl esters of beta-casein"
 FT cleavage_site 201..208
 /note= "newly identified pepsin cleavage site in
 methyl ester of beta-casein"
 FT peptide 2..25
 /label= A
 /note= "tryptic peptide from native protein"
 FT peptide 26..28
 /label= B
 /note= "tryptic peptide from native protein"
 FT peptide 29..32
 /label= C
 /note= "tryptic peptide from native protein"
 FT peptide 33..48
 /label= D
 /note= "tryptic peptide from native protein"
 FT peptide 49..97
 /label= E
 /note= "tryptic peptide from native protein"
 FT peptide 100..105
 /label= F
 /note= "tryptic peptide from native protein"
 FT peptide 106..107
 /label= G
 /note= "tryptic peptide from native protein"
 FT peptide 108..113
 /label= H
 /note= "tryptic peptide from native protein"
 FT peptide 114..169
 /label= I
 /note= "tryptic peptide from native protein"
 FT peptide 170..176
 /label= J
 /note= "tryptic peptide from native protein"
 FT peptide 177..183
 /note= "tryptic peptide from native protein"

FT /label= K
 FT /note= "tryptic peptide from native protein"
 FT peptide 184..202
 FT /label= L
 FT /note= "tryptic peptide from native protein"
 FT peptide 203..209
 FT /label= N
 FT /note= "tryptic peptide from native protein"
 FT modified_site 15
 FT /note= "phosphorylated"
 FT modified_site 17
 FT /note= "phosphorylated"
 FT modified_site 203..209
 FT /note= "phosphorylated"
 PN WO201717518-A1.
 29-JUN-1995.
 20-DEC-1994; F01500.
 23-DEC-1993; FR-015764.
 PA (INRG) INST NAT RECH AGRONOMIQUE.
 PI Briand L, Chobert J, Haertle T;
 WPI; 95-240579/31.
 DR
 PT New esterified amino acids, peptide(s) and their mixts. - prep. by esterification of protein then enzymatic hydrolysis, useful as ingredients and additives in foods, pharmaceuticals and cosmetics.
 Claim 7; Fig 17 and 18; 47 pp; French.
 CC The native form of bovine beta-casein A1 contains various pepsin cleavage sites. Esterification of the protein with methanol or ethanol results in a form of beta casein contg. additional, non-conventional pepsin cleavage sites (see Features Table). Esterified peptides and amino acids (and their mixtures) resulting from hydrolysis of an esterified protein (ref. beta-lactoglobulin or beta-casein) are claimed. The hydrolysis products are useful as ingredients, additives or active agents in foods, pharmaceuticals and cosmetics.
 CC Sequence 209 AA;
 CC 5 A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;
 CC 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
 CC Retrieved by bobjeny on Thu 27 Feb 103 16:22:04 PST using Findseq
 CC
 Initial Score = 11
 Residue Identity = 918
 Optimized Score = 11
 Significance = 1.06
 Matches = 11
 Significance = 1.06
 bobjeny@csan
 Significance = 1.06
 Significance = 1.06

3. US-09-095-639A-4 (1-12)
 aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

ID	AAR95609 standard; protein; 209 AA.
XX	AAR95609;
AC	
XX	
XX	
DT	26-NOV-1996 (first entry)
XX	Bovine beta casein A1 variant.
DE	
XX	
KW	Milk; beta casein; diabetogenic; diabetes; cow: milk products.

KW bovine beta-casein variant A2 immunogenic peptide motif.

KW A2 variant beta-casein; immunogenic; molecular mimicry; cow; milk product; insulin-dependent diabetes; GLUT2; diet.

KW Bos taurus.

OS Bos indicus.

PN W09724371-A1.

PD 10-JUL-1997.

PF 27-DEC-1996; E05846.

PR 27-DEC-1995; IT-RM0850.

PA (BTOS -) BIOSISTEMA DI SARAPANTI & C SAS PIER LUIGI.

PA (MDI-) MIDIA LTD.

PI Pozzilli, P;

DR WPI; 97-3632/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy.

PT Claim 5; Page 4; 34pp; English.

PS This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes.

CC molecular mimicry. Dietary or pharmaceutical products derived from milk
 CC beta-casein without this motif could be used in diets for the prevention
 CC of insulin dependent diabetes particularly during early infancy.
 SQ sequence 5 AA:
 SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 3 P; 0 S; 0 T; 0 W; 0 Y; 0 V;
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using Findseq

Initial Score =

5

Optimized Score =

5

Significance =

-0.53

Matches =

5

Conservative Substitutions =

0

Mismatches =

0

Gaps =

0

X 10

SLVYPPGPPIP
 |||||
 PGPIP
 X X

US-09-095-639a-4 (1-12)
 aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

ID aaw31288 standard; peptide; 5 AA.

XX aaw31288;

AC aaw31288;

XX DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A2 immunogenic peptide motif.

XX KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

OS Bos indicus

XX PN W09724371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0050.

PA (BIOS-) BIGSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MDI-) MIDIA LTD.

Pozzilli P;

XX DR WPI: 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid sequence position 63-66). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

SQ Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 type: P Check: 1154
 Initial Score = 5 Optimized Score = 5 Significance = -0.53
 Residue Identity = 100% Matches = 5 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0
 X 10
 SLVYPPGPPIP
 |||||
 PGPIP
 X X

11. US-09-095-639a-4 (1-12)
 p02662 Alpha-S1 casein precursor.
 TOIG of: p02662 check: 2471 from: 1 to: 214
 ID CASI_BOVIN STANDARD; PRT; 214 AA.
 AC P02662; Q28048;
 DT 21-JUL-1986 (Rel. 01, Created)
 DT 01-NOV-1990 (Rel. 16, Last sequence update)
 DT 01-MAR-2002 (Rel. 41, Last annotation update)
 DE Alpha-S1 casein precursor.
 GN CSNISL.
 OS Bos taurus (Bovine).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Butheria; Cetartiodactyla; Ruminantia; Peccora; Bovidea;
 OC Bovidae; Bovine; Bos.
 OX NCBI_TaxID-991; [1]
 RN RP SEQUENCE FROM N.A.
 RX MEDLINE=84221403; PubMed=6328443;
 RA Stewart A.F.; Willis I.M.; Mackinlay A.G.; [2]
 RT Nucleotide sequences of bovine alpha-S1- and kappa-casein cDNAs.
 RN NCBI_Acids Res. 12:3895-3907(1984).
 RA Nagaoka M.; Maki M.; Sasaki R.; Chiba R.; [3]
 RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA
 RT clone." [4]
 RL Agric. Biol. Chem. 48:1663-1667(1984).
 RN RP SEQUENCE FROM N.A.
 RX MEDLINE=87049835; PubMed=3022813;
 RA Gorodetski S.I.; Zatkar'ev V.M.; Kyarshullite D.R.; Kapelinskaya T.V.; [5]
 RT "cDNA of cattle alpha-S1-casein: cloning and nucleotide sequence." [6]
 RL Biochimika 51:1641-1648(1986).
 RN RP SEQUENCE FROM N.A.
 RX MEDLINE=92051301; PubMed=1658736;
 RA Koczan D.; Hobom G.; Seifert H.M.; [7]
 RT "Genomic organization of the bovine alpha-S1 casein gene." [8]
 RL Nucleic Acids Res. 19:5591-5596(1991).
 RN RP SEQUENCE OF 55-130 FROM N.A.
 RX MEDLINE=83182023; PubMed=689774;
 RA Willis I.M.; Stewart A.F.; Caputo A.; Thompson A.R.; McKinlay A.G.; [9]
 RT Construction and identification by partial nucleotide sequence
 RT analysis of bovine casein and beta-lactoglobulin cDNA clones.
 RL DNA 1:375-386(1982).
 RN RP SEQUENCE OF 122-214 FROM N.A.
 RX MEDLINE=95178933; PubMed=3838718;
 RA Kiarshullite D.R.; Zatkar'ev V.M.; Gorodetski S.I.; [10]
 RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of
 RL alpha-S1-casein in cows." [11]
 RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).
 RN RP SEQUENCE OF 164-214 FROM N.A.
 RX MEDLINE=94154154; PubMed=1343827;
 RA Chen R.; Wang B.; Zhang Y.; Liu W.; Zhang J.; Lao W.;

"Cloning, mapping, and sequencing of 3' and its flanking region of bovine alpha-s1 casein gene." Chin. J. Biotechnol. 8:235-245(1992).

[8] RT RN SEQUENCE OF 16-214 (VARIANT B). RP RX MEDLINE=72063417; PubMed=4331376;

[9] RT RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.; "Primary structure of bovine alpha-s1 casein. Complete sequence." Eur. J. Biochem. 23:41-51(1971).

[9] RT RN REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D). RP RX MEDLINE=74083545; PubMed=797901;

[10] RT RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.; "Primary structure of alpha casein of bovine beta casein. Correction." Eur. J. Biochem. 40:323-323(1973).

[10] RT RN SEQUENCE (VARIANT D). RP RX MEDLINE=7214459; PubMed=5064450;

[11] RT RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.; "Characterization of genetic variants of alpha-S1 and beta bovine caseins." Eur. J. Biochem. 26:328-337(1972).

[11] RT RN SEQUENCE OF 23-49 (VARIANT A). RP RX MEDLINE=7214459; PubMed=5064450;

[12] RT RA "Localization in the N-terminal part of bovine casein alpha-S1 of a 12-amino-acid deletion that differentiates variant A from variants

RT and C.;
 RT PBERS Lett. 11:109-112(1970).

RL RN [112] SEQUENCE OF 205-214 (VARIANT C). Ribadeau-Dumas B.;
 RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RA "On the localization in the C-terminal sequence of bovine casein
 RT alpha-s1 of a Glu/Gly substitution that differentiates the genetic
 RT variants B and C.";
 RT C. R. Acad. Sci., D, sci. Nat. 268:3133-3136(1970).

RL RN [113] (VARIANT C).
 RP REVISION (VARIANT C).
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;
 RL C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).
 CC -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT
 CC CALCIUM PHOSPHATE.
 CC -1- SUBCELLULAR LOCATION: EXTRACELLULAR.
 CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
 CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.
 CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASPIN FAMILY.
 CC -1- DATABASE: NAME-Worthington enzyme manual; C/CASA.html".
 WWW="http://www.worthington-biochem.com/manual/C/CASA.html".
 CC -1- DATABASE: NAME-Protein Spotlight;
 CC NOTE=Issue 016 of November 2001;
 CC WWW="http://www.expsy.org/spotlight/articles/split016.html".
 CC

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CC EMBL; X00564; CAB57792.1; .
CC EMBL; M33123; AAA30428.1; .
DR EMBL; M38641; AAA30429.1; .
DR EMBL; X59856; CAA42516.1; .
DR EMBL; K01084; AAA30478.1; .
DR EMBL; M38658; AAA622707.1; .
DR EMBL; S72388; AAD14099.1; .
DR PIR; A03106; KAB05B .
DR PIR; A23071; .
DR PIR; S02202; S02202.
DR PIR; S2257; S2257.
DR InterPro; IPR001588; Casein.

DR	Pfam; PF00363; cassins; 1.	DR	PROSTIE; BS00306; CASEIN_ALPHA_BETA; 1.	DR	Milk; Phosphorylation; Signal; Repeat.
KW					
FT	SIGNAL	1	15	ALPHA-S1 CASEIN.	
FT	CHAIN	16	214	ALPHA-S1 CASEIN.	
FT	MOD RES	61	61	PHOSPHORYLATION.	
FT	MOD RES	63	63	PHOSPHORYLATION (IN VARIANT D).	
FT	MOD RES	68	68	PHOSPHORYLATION.	
FT	MOD RES	79	79	PHOSPHORYLATION.	
FT	MOD RES	81	81	PHOSPHORYLATION.	
FT	MOD RES	82	82	PHOSPHORYLATION.	
FT	MOD RES	83	83	PHOSPHORYLATION.	
FT	MOD RES	90	90	PHOSPHORYLATION.	
FT	MOD RES	130	130	PHOSPHORYLATION.	
FT	REPEAT	85	99		
FT	REPEAT	125	140	MISSING (IN VARIANT A).	
FT	VARIANT	29	41	A -> T (IN VARIANT C).	
FT	VARIANT	68	68	G (IN VARIANT C).	
FT	VARIANT	207	207	E -> G (IN VARIANT C).	
FT	CONFLICT	42	42	E -> T (IN VARIANT 3).	
FT	CONFLICT	50	50	P -> L (IN REF. 4 AND 11).	
FT	CONFLICT	95	95	E -> Q (IN REF. 4).	
FT	CONFLICT	143	143	H -> P (IN REF. 5).	
FT	CONFLICT	203	203	H -> D (IN REF. 3).	
FT	CONFLICT	211	212	S -> L (IN REF. 6).	
SQ	SEQUENCE	214 AA;	24329 MW;	F066B8C8AE5828B CR64;	
P02662	Length:	214	February 28, 2003 14:33	Type: P Check: 2	
Initial Score = 5	Optimized Score = 5	Significance = 7			
Residue Identity = 258	Matches = 258	Mismatches = 3			
Gaps = 0	Conservative Substitutions = 0	Mismatches = 0			

PN 10-JUL-1997.
 PD ED05846.
 PF 27-DEC-1995; IT-R00850.
 PR (BIOS-) BIOSISTEMA DI SARAPPANI & C SAS PIER LUIG.
 PA (MIDI-) MIDI LTD.
 PI PIZZOLI P.
 DR WPI: 97-363622/33.
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PT Beta-casein or fragments not showing mimicry with GLUT2 -
 PS Claim 10; Page 6; 34PP; English.
 PS This sequence represents an immunogenic peptide motif found
 PS in beta casein. This motif is capable of mimicking a fragment
 PS of the beta casein. This motif is found in insulin producing cells of the pancreas.
 CC GLUT2 protein found in insulin and the
 CC known correlation between exposure to cow's milk and the
 CC insulin-dependent diabetes which could possibly be linked
 CC to molecular mimicry. Dietary or pharmaceutical products derived
 CC substantially free of non human beta casein or containing
 CC beta-casein without this motif could be used in diets for
 CC insulin dependent diabetes particularly during early life.
 CC sequence 4 AA: N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1
 SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1

SQ 1 I; 0 L; 0 R; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 -PST using FindSeq
 Initial Score = 4 Optimized Score = 4 Significance = -0.80
 Residue Identity = 100% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

10
 SLVYPPGPIP
 |||||
 GPIP
 x x

13. US-09-095-639A-4 (1-12)
 aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.

AAW31294;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein immunogenic peptide motif 2.

XX XX

Beta-casein; immunogenic; molecular mimicry; cow;
 milk product; insulin-dependent diabetes; GLUT2; diet.
 XX OS Bos taurus.

XX PN WO9724371-A1.

XX PD 10-JUL-1997.

XX PF 96WO-EP05846.

XX PR 27-DEC-1995; 95TT-0RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.
 (MDI-) MIDIA LTD.

XX PI Pozzilli P;

XX WO97-363622/33.

XX DR 10-JUL-1997.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp. English.

XX CC This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this

CC molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 5 AA;

XX SQ 0 A; 0 F; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 2; 1 G; 1 H;

XX SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

XX CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 -PST using FindSeq

XX ID Initial Score = 4 Optimized Score = 4 Significance = -0.80
 Residue Identity = 80% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

XX SQ Sequence 4 AA;

XX AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

XX Initial Score = 4 Optimized Score = 4 Significance = -0.80
 Residue Identity = 100% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

XX SQ Sequence 4 AA;

XX AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

XX ID WO9724371-A1.

XX PD 10-JUL-1997.

|||||
 GPIP
 x x

14. US-09-095-639A-4 (1-12)
 W31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide; 5 AA.
 AC W31287;
 DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A1 immunogenic peptide motif.
 KW A1 variant beta casein; immunogenic; molecular mimicry; cow;
 KW milk product; insulin-dependent diabetes; GLUT2; diet.
 OS Bos taurus.

XX PN WO9724371-A1.

XX DR 10-JUL-1997.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 3; 34pp. English.

CC This sequence represents an immunogenic peptide motif from the A1 variant of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

CC Sequence 5 AA;

CC SQ 0 A; 0 F; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 2; 1 G; 1 H;

CC SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

CC CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 -PST using FindSeq

CC ID Initial Score = 4 Optimized Score = 4 Significance = -0.80
 Residue Identity = 80% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

XX X 10
 SLVYPPGPIP
 |||||
 GPIP
 x x

15. US-09-095-639A-4 (1-12)
 aaw31287 Bovine beta casein variant A1 immunogenic peptide
 TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide; 5 AA.

XX AC AAW31287;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A1 immunogenic peptide motif.
 KW A1 variant beta casein; immunogenic; molecular mimicry; cow;
 KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN WO9724371-A1.

XX PD 10-JUL-1997.

XX SQ Sequence 4 AA;

XX AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

XX Initial Score = 4 Optimized Score = 4 Significance = -0.80
 Residue Identity = 100% Matches = 4 Mismatches = 0
 Gaps = 0 Conservative Substitutions = 0

XX SQ Sequence 4 AA;

XX AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

XX ID WO9724371-A1.

XX PD 10-JUL-1997.

KW milk product; insulin-dependent diabetes; GLUT2; diet.
 XX Bos taurus.
 XX WO0724371-A1.
 XX 10-JUL-1997.
 XX 27-DEC-1996; 96WO-EP05846.

XX 27-DEC-1995; 95IT-ORM0850.
 XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.
 PA (MIDI-) MIDIA LTD.
 XX PI Pozzilli P;
 XX DR WPI; 1997-363622/33.

XX PR Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp; English.

XX CC This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738
 Initial Score = 3 Optimized Score = 3 Significance = -1.06
 Residue Identity = 75% Matches = 3 Mismatches = 1
 Gaps = 0 Conservative Substitutions = 0

10
 SLVYPPPGPPIP
 |||
 GPRH
 X X

